

Consortium for Materials Development in Space

FY '99 Annual Report

September 10, 1999

CONSORTIUM FOR MATERIALS DEVELOPMENT IN SPACE
University of Alabama in Huntsville
Huntsville, AL

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1.0 INTRODUCTION

During FY99 the Consortium for Materials Development in Space (CMDS) was reorganized around the following guidelines: industry driven, product focus, an industry led advisory council, focus on University of Alabama in Huntsville (UAH) core competencies, linkage to regional investment firms to assist commercialization and to take advantage of space flights.

The organizational structure of the CMDS changed considerably during the year. The decision was made to reduce the organization to a Director and an Administrative Assistant. The various research projects, including the employees, were transferred to the appropriate UAH research center or college. In addition, an advisory council was established to provide direction and guidance to the CMDS to ensure a strong commercial focus. The council will (i) review CMDS commercial development plans and provide feedback, (ii) perform an annual evaluation of the Center's progress and present the results of this review to the UAH Vice President for Research, (iii) serve as an avenue of communication between the CMDS and its commercial partners, and (iv) serve as an ambassador and advocate for the CMDS.

Current members of the CMDS Advisory Council are:

- James R. Hudson Jr., President (Advisory Council chair)
Research Genetics, Inc., Huntsville, AL
- Milton Harris, President
Shearwater Polymers, Inc., Huntsville, AL
- Tom Dooley, President
IntegriDerm, Inc., Birmingham, AL
- Timothy E. Taylor, Director of Investments
Harbert Management Corp., Birmingham, AL
- Lawrence R. Greenwood, Vice President for Research, UAH
- Mark Nall
Space Product Development Office, Marshall Space Flight Center
- William Gathings, Director
Consortium for Materials Development in Space, UAH

2.0 PAYLOADS FLOWN

The following shuttle payloads were flown:

- Acceleration measurement devices on STS-95 under contract from Spacehab.
- Tissue engineering – bone implant development experiment on STS-95 with industrial affiliate, Millenium Biologix, Inc.
- Protein products from cells – cell aging factor experiment on STS-95 with industrial affiliate, Synthecon, Inc.
- Anti-cancer and anti-alcoholism products from plant cells on STS-95 with industrial affiliate, Huaser Chemical, Inc.
- Protein dehydratase crystallization experiment on STS-95 as part of DeLucas guest investigator program.

The SPDEM/ISS facility is currently manifested for UF-3, which is scheduled for launch in February 2003.

The NLO-PVT and NLO-PTFG are manifested on flight 12A.1 in December 2001 according to the Rev. D' schedule.

The CONCAP IV-4 is manifested for STS-105 in November 2000 as part of H.E.A.T.

3.0 COMMERCIAL ACTIVITY

No new spin-off firms were formed in 1999.

3.1 Research Genetics, Inc.

An exclusive technology licensing/royalty agreement was signed with Research Genetics, Inc., Huntsville, Alabama. This commercialization agreement covers sets of genes that encode proteins associated with the processes of bone formation and resorption, or biomineralization. These so-called 'unigene sets', which were isolated and defined in the Laboratory for Structural Biology (LSB) at UAH, will form the basis for commercial development of a GeneFilters™ high throughput screening microarray for studying gene expression.

The UAH LSB also plans to produce a panel of recombinant biomineralization proteins for commercialization. Research Genetics has agreed in principle to serve as a commercial outlet for these products. CMDS will also investigate OEM sales to other firms (e.g., Sigma Chemical, Boehringer Mannheim, Wako).

NOTE: GeneFilters™ is a registered trademark of Research Genetics, Inc., Huntsville, AL

3.2 Shearwater Polymers, Inc.

Shearwater Polymers, Inc., Huntsville, Alabama is our commercial research partner for development of peg-y-lated biomineralization proteins that may have utility for treatment of diseases of bone and cartilage. While this study will not be initiated until late 2000, members of the research teams from the LSB and Shearwater are now meeting on a biweekly basis to discuss development strategy. At the present time, no formal agreements are in place with Shearwater. The CMDS is currently drafting both a Dual Party Non-Disclosure Agreement and a Collaborative Research Agreement for company review. These Agreements are to ensure both protection and disposition of any intellectual property/technology resulting from the collaboration.

4.0 MILESTONES

The following projects were supported by the CMDS during the year:

4.1 Biomineralization

4.1.1 Development of Gene Filters™ Microarray

Project manager: Ed Meehan, Director of the Laboratory for Structural Biology, UAH

Collaborators: None

Industry partner: Research Genetics, Inc., Huntsville, AL

Status: Project ongoing

Work is proceeding toward development of a working prototype of the GeneFilters™ microarray for evaluation of genes encoding proteins associated with biomineralization. We anticipate that the prototype will be completed in early 2000, with product launch scheduled for the 2nd quarter of 2000. Research Genetics has an established product line of DNA microarrays and the proposed biomineralization array is an extension of this successful product line.

The following milestones have been met:

- DNA library search for genes encoding biomineralization proteins completed; 5/99
- RNA samples from five different states of differentiation of an osteoblast cell line received from Dr. Kumar at the Mayo Clinic; 6/99
- Large-scale hybridization study utilizing total RNA from the osteoblast cell lines and existing GeneFilters™ microarrays conducted; 6/99
- Analysis of the large amount of data generated by the hybridization study initiated; 7/99
- Gene sequences for creation of expression library selected and verified; 7/99

- List of genes to be bound to the biomineralization GeneFilters™ completed; 7/99
- Cloning of cDNAs and creation of expression library initiated; 8/99

4.1.2 Production of Recombinant Biomineralization Proteins

Project manager: Ed Meehan, Director of the Laboratory for Structural Biology, UAH

Collaborator(s): Dr. Magnus Hook, University of Texas, Houston Medical Center, Houston, TX
Dr. V. Kumar, Mayo Clinic & Foundation, Rochester, MN
Dr. Murat Karpensky, Institute of Molecular Biology, Russian National Academy of Sciences, Moscow, Russia

Industry partner(s): Research Genetics, Inc., Huntsville, AL; others possible

Status: Project ongoing

A great deal of effort is being expended toward gene cloning, construction of expression vectors, eukaryotic protein expression in prokaryotic systems, recombinant protein production, and protein purification and characterization. Collaborations have been established with a number of university investigators to procure some of the starting materials. The goal is to develop and manufacture a panel of purified recombinant proteins that play a role in bone/cartilage formation and resorption. As a result of delays in receipt of equipment for the protein expression facility, the schedule has been pushed forward by 1-2 months. The following milestones have been reached:

- Cloned expression vectors for human and rat osteopontin received; 5/99
- Cloned genes for human protein tyrosine phosphatase-1b received and DNA primers for construction of expression system ordered; 6/99
- Expression vectors for human protein tyrosine phosphatase-1b created; 7/99
- Crystallization studies of calbindin initiated; 7/99
- Facility for protein expression, purification and characterization fully equipped; 8/99
- Human protein tyrosine phosphatase-1b and rat osteopontin successfully expressed, produced and purified; production optimization studies continue; 8/99
- Crystallization of human protein tyrosine phosphatase-1b and rat osteopontin initiated; 9/99

4.1.3 Production of Peg-Y-Lated Biomineralization Proteins

Project manager: Ed Meehan, Director of the Laboratory for Structural Biology

Collaborator(s): Not determined

Industry partner(s): Shearwater Polymers, Inc., Huntsville, AL

Status: Strategic planning sessions only; project to be initiated in late 2000

4.1.4 Development of Designer Drugs

Project manager: Ed Meehan, Director of the Laboratory for Structural Biology

Collaborator(s): DeLucas, UAB
Carter, New Century
Ciszak, MSFC-LSB
McPherson, UC-Irvine
Wang, UGA

Industry partner(s): Shearwater Polymers, Inc., Huntsville, AL

Status: Project to be initiated in late 2000

4.2 Vapor Transport Crystal Growth (VTCG)

Project manager: Robert Naumann, Director of the Alliance for Microgravity Materials and Science Applications

Collaborator(s): William Powell, MSFC

Industry Partner(s): Northrup Grumman, Inc.
Brimrose Corporation of America, Baltimore, MD

Status: Project ongoing.

The following milestones were completed:

- Confinement facility completed 9/98
- VTCG furnace fabrication completed; 2/99
- First and second mercurous chloride crystal grown; 4/99 & 7/99, respectively
- Mercurous chloride crystals analyzed
- Multiple sublimation purification facility fabrication completed; 6/99.
- Multiple sublimation chamber redesigned and fabricated; 8/99

4.3 Non Linear Optical (NLO) Materials

Project manager: Maria Zugrav, Sr. Research Scientist in the Center for Microgravity and Materials Research.

Collaborator(s): Donald Frazier, MSFC

Industry Partner(s): Optron Systems, Inc./R21

Status: Project ongoing

The completed milestones are:

- Optron requirements for UAH organic thin film process defined; 6/99

Dr. Aly Ersen of Optron, our industrial partner, expressed through Dr. Don Frazier of MSFC an interest in working with DCVA thin films deposited on specific substrates as soon as they become available. All available substrates that are of interest to Optron are integrated into the CONCAP IV-4 payload. Efforts are underway to secure more of the desired substrates for deposition onto thin films for Optron to study.

- Wide-band material for PVT process (e.g., TPS) obtained; 6/99

Approximately 0.5 g of triethylphosphine sulfide (TPS) were obtained from Dr. Mohan Aggarwal of Alabama A&M University through arrangements made by Dr. Frazier. Dr. Frazier has identified TPS as being suitable for applications as a wide-band second order NLO material.

- PVT cell for wide-band thin film fabricated; 8/99

Considerable efforts have gone into preparations for attempting to grow wide-band thin film including:

1. Assembly of new Physical Vapor Transport (PVT) facility including the vacuum bench to accommodate more than one experiment simultaneously - The existing facility consists of one PVT oven that is dedicated to the growth of DCVA (N, N-dimethyl-p-(2, 2 dicyanovinyl aniline), which is the first NLO material of interest to Optron.
 2. Assembly of an additional PVT oven to accommodate the PVT cell for wide-band thin film - Built up and is ready to use a new controller card, including power switching, signal conditioning, and data acquisition circuits for the new PVT facility.
 3. Fabrication of PVT cell for wide-band thin film
- Optical non-linearity for lab DCVA thin films determined; 8/99

To meet this milestone it was necessary to master the novel PVT thin film growth process, demonstrated in the laboratory for the first time in January 1999. While much progress has been made, we are still struggling with reproducible growth of thin DCVA films on copper substrates and are not as yet capable of growing films of a particular thickness on demand. As reported in August a major breakthrough in the

crystal growth process has been made. We have established two thresholds behind which we must stay in order to grow these films. The first is a threshold for background nitrogen pressure and the second is the temperature difference, ΔT , between source material and substrate. At least one additional factor exists which affects film growth but is not readily apparent to us. We observed that, under the same growth conditions of nitrogen pressure and ΔT , one experiment resulted in good film growth but, in a second experiment, films did grow not at all. As a result, we have submitted only one film for second harmonic generation (SHG) evaluation. SHG is the method used to evaluate optical non-linearity.

- Current lab DCVA thin film thickness on profilometer measured; 8/99

Measurement of thin film thickness by profilometry is a destructive test and will be done only after non-linearity characterization has been completed.

- First laboratory run of wide-band thin film completed; 9/99

The only remaining item required before operations can begin is the vacuum system. The machine shop is welding the last components for the vacuum system. When the welding is finished and the system leak-checked by a Varian field engineer, the first PVT experiments involving the new wide-band material will be initiated.

Completed milestones for the CONCAP IV-4 are:

- CRP, PIP and ICD submitted to GSFC; 5/99
- Phase 2 flight safety data package submitted; 8/99

Completed milestones for NLO Station hardware are:

- Preliminary Phase 0/1 Flight Safety Data Packages submitted
- Preliminary EXPRESS Integration Agreements submitted
- Payload Verification Plans in development
- PDR planned for Spring 2000

4.4 Acceleration Measurements

Project manager: Jan Bijvoet, Sr. Research Scientist (retired) in the CMDS

Status: Project completed. A report on the project is given in Appendix A.

4.5 Biodynamics

Project manager: Marian Lewis, Research Professor of Biological Sciences

Status: Project completed. STS-95 BioDyn payloads were 100% successful. All of the stated mission objectives were met including verification of the automated cell culture systems (ABPM and BioDyn bioreactor). The final report is given in Appendix B.

4.6 Sintered and Alloyed Metals

Project manager: James Smith, Professor of Chemical and Materials Engineering

Status: Project completed. The six-month report is given in Appendix C. The final report is scheduled for completion by October 31, 1999.

4.7 Space Products Division Experiment Module (SPDEM)

Project manager: Gary Workman, Sr. Research Scientist in the Center for Automation and Robotics.

Status: Project ongoing. Documentation required for the Integrated Payload PDR has been developed and delivered.

Primary deliverables are:

- Preliminary Structure Assessment Plan; 5/99
- Preliminary Fracture Control Plan; 5/99
- Preliminary Training Requirements; 8/99
- Preliminary Ground Data Services Document; 8/99
- Preliminary Payload Operations Requirements; 8/99
- Preliminary Payload Operations Requirements; 8/99
- Preliminary Payload Planning Requirements; 8/99
- Preliminary KSC Support Requirements; 8/99
- Preliminary Phase 0/1 Safety Document; 8/99
- Preliminary Structural assessment and NASTRAN model delivered; 9/99

The Integrated Payload PDR is now scheduled for February 2000.

4.8 Low Temperature/Low Energy Carrier

Project manager: Francis Wessling, Professor and Chair in the Department of Mechanical and Aerospace Engineering.

Status: Project ongoing. Hardware development preliminary design review; 5/99.

The project has two elements. The first consists of developing a passive carrier that requires no energy to transport biological samples to and from the ISS. Research has begun on the various types of active cooling mechanisms for the second element of the project. The technology developed by Space Hardware Optimization Technology (SHOT) under a NASA SBIR fits well with the design for the active carrier portion of the project. Plans are to include SHOT as a partner in the project.

5.0 PATENTS

In 1987 UAH filed a patent for the first material discovered to be superconducting above the temperature of liquid nitrogen. This application has been the subject of an interference proceeding in the U.S. Patent and Trademark Office. UAH was notified in 1999 that it had lost the interference and has asked for a review.

In 1997 UAH received notice that a patent "High temperature processing of cuprate oxide superconductors" was ready for issue in Canada. Canadian patent 1339720 was issued in March 1998.

Two abstracts describing the invention for the electrodeposition project were combined by the attorneys into a single filing titled "Modified brushite surface coating process therefore, and low temperature conversion to hydroxapatite." The number is 08/980,839 with an initial filing date of December 1, 1997. The filing is still under review.

An internal invention disclosure was signed in May 1999 for a novel technique for growing organic thin films.

6.0 PUBLICATIONS

The following manuscripts were either published or are in press in referred journals:

Biom mineralization

Setzer, W.N., G.J. Grant, E.J. Meehan, S.D. Lee, R.M. Kirk, C.R. Yang, and C.K. Wu. The crystal structure of the macrocyclic hexathioether 1,4,7,11,14,17-hexathiocycloeicosane: Implications for metal complexation. *J. Inclusion Phenomena Molec. Rec.*, 1999, in press.

Karpova, A., E.J. Meehan, M.L. Pusey, and L. Chen. Crystallization and preliminary x-ray diffraction analysis of restriction endonuclease EcoRII, elisavate. *Acta. Cryst. D.*, 1999, in press.

Setzer, W.N., M.C. Setzer, R.B. Bates, P. Nakkiew, B.R. Jackes, L. Chen, M.B. McFerrin, and E.J. Meehan. Antibacterial hydroxycinnamyl esters from *P. caninum* from

Paluma, North Queensland, Australia. The Crystal and molecular structure of bornyl coumarate. *Planta Medica*, 1999, in press.

Su, L., L. Chen, M. Egli, J.M. Berger, and A. Rich. Minor groove RNA triples in the crystal structure of a ribosomal frameshifting viral pseudoknot. *Nature Structural Biol.*, 1999, in press.

Sauter, C., J. Ng, B. Lorger, G. Keith, P. Brion, M.W. Hosseini, J.-M. Lehn, and R. Giege. Additives for the crystallization of proteins and nucleic acids. *J. Cryst. Growth* 196:365-376, 1999.

Biodynamics

Lewis, M.L., J.A. Reynolds, L.A. Yancey, B.D. Lawless, and E.H. Piepmeier. The cell death factor, sFas/APO-1, as a regulatory mechanism of apoptosis and population growth response in space flown lymphocytes. *Gravitational and Space Biology Bulletin*, 12, 1998.

Sintered and Alloyed Metals

Naser, J., A. Kuruvilla, and J. Smith. Effect of microgravity on grain coarsening during liquid phase sintering in the Fe-Cu system. *J. Mater. Sci.* 33, 5573-5580, 1998.

The following papers were published in non-referred journals and conference proceedings:

Sintered and Alloyed Metals

Odojin, D., and J. Smith. Macrostructural and microstructural analysis of ejected beads from microgravity liquid phase sintered Fe-Cu alloys. *Tri-State Engineering Societies Meeting Student Paper Competition Proceedings*, Sandestin, Destin, FL, pp. 1-6, June 1999.

Riley, M., S. Noojin, and J. Smith. Commercial opportunities for the on-site use of the extreme temperature translation furnace. *Space Technology & Applications International Forum (STAIF-99)*, Albuquerque, NM, January 1999.

Naser, J., Y. Ye, S. Kuruvilla, and J. Smith. LSW, LSEM and mean field theory distributions for Fe-Cu LPS microgravity results. *Proceedings of 11th International Symposium on Experimental Methods for Microgravity Materials Science*, February 1999.

He, Y., S. Ye, J. Naser, J. Chiang, and J. Smith. Diffusion effects on liquid phase sintered Co-Cu samples in microgravity. *Proceedings of 11th International Symposium on Experimental Methods for Microgravity Materials Science*, February 1999.

Naser, J., and J. Smith, Martin E. Glicksman Modification of the LSEM model to utilize local volume fraction and shape factor for highly agglomerated microgravity processed LPS systems Symposium on Solidification and Crystal Growth. *Proceedings of 11th International Symposium on Experimental Methods for Microgravity Materials Science*, February 1999.

Naser, J., Y. He, S. Ye, and J. Smith Transport effects in microgravity processed multi-phase composites. *Proceedings of XVIII Interamerican Congress of Chemical Engineering*, San Juan, P.R., December 1998.

Hamilton, T., and J. Smith. Thermal and mechanical performance of TTZ zirconia helical ceramic springs. *Proceedings of XVIII Interamerican Congress of Chemical Engineering*, San Juan, P.R., December 1998.

Smith, J. Optizone liquid phase sintering experiment OLIPSE-02. *Proceedings Phase I Research Program Interim Results Symposium*, Microgravity and Materials Sciences Section, Huntsville, AL, November 1998.

Non-Linear Optics

Zugrav, M., J. Carswell, and F. Wessling. Vapor transport growth of organic crystals: morphology vs. microgravity. *XVIIIth International Union of Crystallography Congress*, Glasgow, Scotland, August 4-14, 1999.

Carswell, J., M. Zugrav, F. Wessling, and J. Haulenbeek. An evaluation of single-crystalline organic thin films grown on STS missions. *11th American Conference on Crystal Growth and Epitaxy*, Tucson, AZ, August 1-6, 1999.

Space Products Division Experiment Module

Watson, C., C. Lundquist, F. Wessling, J. Smith, and R. Naumann Space product development experiment module using the ISS, *Space Technology & Applications International Forum (STAIF-99)*, Albuquerque, NM, January 1999.

Other

Lundquist, C.A. Materials development opportunities. *Space Technology & Applications International Forum (STAIF-99)*, Albuquerque, NM, January 1999.

Naumann, R.J., and G. Halebeek. Japanese-US thermal science accelerometer project. *Space Technology & Applications International Forum (STAIF-99)*, Albuquerque, NM, January 1999.

The following presentations (excluding the above-cited papers) were made:

Lewis, M.L., J.A. Reynolds, L.A. Yancey, B.D. Lawless, and E.H. Piepmeier. The cell death factor, sFas/APO-1, as a regulatory mechanism of apoptosis and population growth

response in space-flown lymphocytes. *Gravitational and Space Biology Bulletin*, 12, 1998.

Carswell, J. Invited to represent materials processing in space on panel. Doing business on the space station. *8th Annual Space Frontier Conference*, Los Angeles, CA, September 1999.

Carswell, J., Paley, and D. Frazier. Invited to discuss "Polymer thin film growth (PTFG) in microgravity," *219th ACS National Meeting*, San Francisco, CA, March 1999.

Book contribution:

Zugrav, M., W. Carswell, and F. Wessling. Ground and space processing of nonlinear optical organic Materials. Invited paper submitted to *Recent Developments In Crystal Growth research*, published by Transworld Research Network, Editorial Advisors K. Benz, D. Schwabe and I. Higashi. In preparation

7.0 DEGREES AWARDED

Students employed through CMDS who graduated this year are:

K.H. Sarwa Bakti Ta, M.S.

Thesis: "Purification and closed tube vapor growth of mercurous chloride single crystals"

Amy Russell, BS

Y. He, M.S.

Thesis: "Microstructure evolution of liquid phase sintered Co-Cu samples in microgravity"

J. Naser, Ph.D.

Dissertation: "Grain growth kinetics modeling in microgravity liquid phase sintering"

8.0 FORMAL PRESENTATIONS TO INDUSTRY

The following presentations were made to industry:

- August 99 – Presentation to Space Hardware Optimization Technology (SHOT) on its participation in the low temperature/low energy carrier. SHOT and CMDS have agreed to cooperate on the carrier development.
- April 99 – Presentation to Brimrose Corporation, Baltimore, MD. Discussed the anticipated relationships for spaced product development and achieved common understanding of goals for commercial applications of mercurous chloride. The

current agreement is still in effect. No changes anticipated until preparations for launch ramps up closer to launch.

- April 99 – Presented the CONCAP hardware at the Spring Technical Interchange Meeting at GSFC. Payload and the requirements for a successful mission were discussed which enabled us to become familiar with the other payloads involved with H.E.A.T. mission.
- Discussions were held with Dr. Ron Clark, Director of the Alliance for Non-Linear Optics about the CMDS providing a commercial arm for them. Two potential advisors have been submitted to the alliance to strengthen their commercial thrusts: Dr. Jim Trolinger from MetroLaser, Inc. and Fred Way from Decade Optics

9.0 NEWS ARTICLES

No significant news articles were published on CMDS activities.

10.0 EMPLOYEES

Dr. William Gathings became the new director effective August 30, 1999. He holds a Ph.D. in immunology from the University of Alabama in Birmingham. Prior to joining CMDS, he was president and scientific director of Southern Biotechnology Associates, Inc., a company he founded in 1982. He has a proven track record in product development and commercializing technology. Dr. Bernard J. Schroer became the interim director in January 1999, following the retirement of Dr. Charles A. Lundquist. Effective the fall 1999 semester, Dr. Francis Wessling, Associate CMDS director, resigned to become the Chair of the Department of Mechanical and Aerospace Engineering at UAH.

Ms. Linda Jones is the administrative assistant. Ms. Jones has been a CMDS employee for a number of years and provides the requisite knowledge for administrative, reporting, and budget matters in the CMDS.

The remaining CMDS employees were transferred to their various research centers and academic departments that are supporting CMDS research. During the year the CMDS supported:

17.25 FTE employees
6 undergraduate students
10 graduate students

Maria Zugrav was selected as a female role model by the SD10/Manager in Microgravity Research Program Office for significant contributions made to NASA's Microgravity Research and Space Product Development Programs. The activity included a Web page to encourage young women to consider a career in science or engineering.

APPENDIX A

Acceleration Measurements Report

Three Dimensional Microgravity Accelerometer 3-DMA

Jan A. Bijvoet

April, 1999

THREE DIMENSIONAL MICROGRAVITY ACCELEROMETER

3 - D M A

APRIL 1999

MISSIONS and FLIGHT EXPERIENCE (1989 - 1998) (Fig.1):

- ORBITER: 7 Shuttle missions
 - 5 SPACEHAB Missions (STS-57/60/63/79 and 95).
 - SPACELAB MISSION (STS-73) (USML-02).
 - REAL - TIME ACCELERATION DATA TO PI's ON THE GROUND (STS-73).
 - ADVANCED PROCESSING & CONTROL UNIT AND SIX SENSOR UNITS PROVIDED TO ARIS PROGRAM (ACTIVE RACK ISOLATION SYSTEM)
 - VERY SMALL SYSTEM FOR CFZF (CANADIAN FLOAT ZONE FURNACE)
 - ACCELEROMETER IN GET-AWAY-SPECIAL FOR TETHER MISSION(STS-46)
- SUBORBITAL ("Free Flyers") :
 - 8 SOUNDING ROCKET FLIGHTS ;
 - APRIL "96: FIRST AUTONOMOUS "FREE FLYER", PC-104 UNIT on "CONQUEST 1".
- SPACECRAFT:
 - VERY SMALL UNIT PROVIDED TO METEOR / COMET

SEVERAL 3-DMA VERSIONS - ADAPTATED TO MISSION

NEW SMALL, AUTONOMOUS, UNIT

VERY LOW COST

CONTACT : Jan A. Bijvoet ('byfoot'),
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Tel.: 1(256) 883 1134

THREE DIMENSIONAL MICROGRAVITY ACCELEROMETER (3 - DMA)

VERSIONS:

3 - DMA systems are available for flight in different versions, large and small, and with different functions depending on experimenter- or mission manager- requirements and matching available platform facilities. Examples of some configurations are given in Figure 2. A Remote sensing Unit (RU) and a Data Recording Unit (DRU) are shown in Figures 3 and 4.

THE SIMPLEST VERSION USES ONE RU (NO DRU) AND REAL-TIME DATA TRANSMISSION TO THE GROUND.

The earlier, large, locker-housed Central Processing Unit (CU) is NOT needed anymore. Instead a small Data Recording Unit (DRU) has been built and validated in flight. The DRU has all the processing and recording capability of the earlier flown CU.

Configurations can comprise one or more or all of the following elements:

- One or more 3 - Dimensional "Remote Unit" sensors (RU), with internal signal conditioning circuits, for measurement of microvibrations and transients at locations desired by Investigators or by the platform provider.
- Data processing and data Recording Unit (DRU) with or without full Data Recording and with or without real-time Telemetry to the ground of all data or of selected or preprocessed microgravity data. Three or more RU's can be served by one small data processor / data recording unit .
- "Invertable Accelerometers" (I.A.) for the measurement of quasi-stationary and absolute acceleration levels by elimination of bias errors. (Measurement of absolute acceleration is necessary for the measurement of residual quasi-stationary very low frequency gravity levels; otherwise the inherent bias variations give false readings).

REAL-TIME MICROGRAVITY DATA TO THE GROUND:

We introduced transmission of full acceleration data to the ground in real time for the STS-73/Spacelab (USML-02) Shuttle mission. All acceleration data measured by 3-DMA were transmitted via the Spacelab wide-band High Rate Multiplexer to the Payload Operations Control Center (POCC) at NASA MSFC. Selected 3-DMA data channels were distributed via the Video Matrix to Principal Investigators and the Mission Scientist.

The Mission Manager of the US Payload on the Spacelab / STS- 73 mission wrote: "The use of your real-time acceleration data, in conjunction with the operation of the Surface Tension Driven Convection Experiment, demonstrated the need for this type of operation on future flights". (See copy of letter attached, Fig.3).

If a wide-band link is not available, preprocessed data and status information and/or a selected channel with full raw acceleration data can be sent via the narrow-band link from SPACEHAB to the ground or recorded on board.

At Sounding Rocket missions, all acceleration data are sent real-time to the ground via a mission-provided telemetry system.

NEED FOR MICROGRAVITY MEASUREMENTS:

When experimenting in space or processing materials samples and exploiting the very low acceleration environment, measurement of the very low microgravity levels down to one micro-g ($10E-6$ g) relative to the gravity on Earth is necessary for the following reasons:

Just as experiments performed at very low temperatures require adequate measurement of the actual temperatures, experiments in low gravity require measurement of the acceleration levels of the many different disturbing components such as high or low frequency vibrations, transients, drag-induced decelerations etc., each of which may have a different effect on a process in low-g.

The levels of the different components of "THE" microgravity environment need to be quantified and the sources of the disturbances identified.

A Principal Investigator needs this information to be able to :

- Reproduce his experimental results
- Determine the threshold of those microgravity component(s) below which the measured (desired) effect occurs.
- Determine the actual levels of microgravity needed.

Additional controlled experiments in known and/or in induced acceleration environments are needed.

The measurement of the different microgravity disturbing components is also needed :

- to determine the disturbances generated by experiments themselves that may influence other experiments on board and
- to verify that the space platform meets specified maximum acceptable acceleration levels.

The 3-DMA system has been designed to meet these needs in relation to the commercial development of materials processing in space.

In this context the 3-DMA has been developed as very low cost and marketable instrumentation.

MEASUREMENT SENSITIVITY:

All Remote Units and Invertable Accelerometer Units measure acceleration in three orthogonal axes.

In addition in each acceleration axis simultaneously and continuously acceleration is measured in three frequency bands and with correspondingly higher measurement sensitivities. The three frequency bands and corresponding sensitivities (see below) are tailored to the spectrum of disturbances normally encountered on Orbiter missions and to Space Station requirements.

The accelerometer noise level in the sensitive "Fine" channel (0-1Hz) as derived from manufacturer's measured noise data is only $0.07 \mu\text{g}$ ($7 \times 10^{-8} \text{ g}$).

A ten times sensitivity increase was introduced in conjunction with bias control.

During a very quiet Sounding Rocket flight in April 1966 we have been able to validate by measurement a system sensitivity below one micro-g.

Scale Factors, Measurement Ranges and the inherent Accelerometer Noise Levels for the three simultaneous channels are shown in the table below.

THREE, SIMULTANEOUS, FREQUENCY BANDS:

Accelerations are measured simultaneously and continuously in three frequency bands by all accelerometers and associated signal conditioning circuits.

There is no need therefore to be limited to only one frequency range per Remote sensing Unit or to have to specify the frequency band required from a Remote Unit or Invertable Accelerometer before flight or to select a band in flight.

The simultaneous availability of multiple frequency bands permits proper handling of the "DC", very low level, very low frequency deviations in the simultaneous presence of the high frequency very high level disturbances normally encountered on a space platform.

TABLE OF SIMULTANEOUS FREQUENCY BANDS, SENSITIVITIES AND RANGES.

CHANNEL	FREQUENCY BAND	NOISE LEVEL	SCALE FACTOR	MAXIMUM RANGE
"Fine"	0 - 1 Hz	$0.07 \mu\text{g}$	$50 \text{ mV} / \mu\text{g}$	$\pm 200 \mu\text{g}$
"Medium"	0 - 10 Hz	$0.45 \mu\text{g}$	$5 \text{ mV} / \mu\text{g}$ or $5 \text{ V} / \text{milli-g}$	$\pm 2 \text{ milli-g}$
"Coarse"	0 - 300 Hz	$34 \mu\text{g}$	$0.5 \text{ V} / \text{milli-g}$	$\pm 20 \text{ milli-g}$
Or for Lift-Off measurements can be set for e.g.: $0.5 \text{ V} / \text{g}$				and $+6 \text{g}$ to -10g

Note: 0 Hz is actual zero frequency, or "DC", for registration of changes of the quasi-stationary acceleration levels.

SAMPLING RATE:

The sampling rate is selectable. Values used at the STS 95 mission were 45 and 600 Samples / second.

AUTOMATIC DATA RECORDING:

The earlier SPACEHAB- and Spacelab Missions and the Unit developed for the Boeing ARIS employed Hard Disk Drives for storage of all mission acceleration data.

We have validated that Hard Disk Drives perform excellently on orbit.

Automatic switch-over from drive to drive was introduced.

Therefore no routine crew actions are needed to exchange data recording elements on these systems and crew operations are basically limited to Switch On at the beginning of a mission and Switch Off before reentry; and: no interruption of data recording is necessary during module close down for Extra Vehicular Activities (EVA). No supplementary stowage of data recording elements is needed.

All data has been recorded for full duration Shuttle missions.

HIGH-G ASCENT AND ON ORBIT MICRO-G WITH THE SAME INSTRUMENT:

The Course channels of the accelerometers can be configured for the measurement of the high accelerations at vehicle Ascent and at Landing. The software is specially programmed to save the data from shortly before lift-off through ascent. On orbit, micro-g levels are measured with the Medium and Fine Acceleration Channels.

DATA DISPLAY ON BOARD:

On orbit, the crew can hook up a Laptop computer to the DRU and display acceleration data in real time on orbit.

ACCELEROMETER:

Early in the program the Allied Signal (formerly Sundstrand) QA-3000-10 accelerometer was chosen, because of its better bias stability over the QA-2000.

The QA Accelerometers are Servo Accelerometers and therefore have an essentially linear response to acceleration.

Non-linear accelerometers, such as those employing the piezo-electric effect and other non-servo type accelerometers produce false "DC" and low frequency responses due to signal rectifying in the typical on-orbit environment of low frequency very low accelerations in the presence of high frequency high level disturbances.

EXAMPLES OF DATA:

Examples of acceleration and frequency data from different missions are attached.

ACCOMMODATION:

Low power: 3.5 Watt (at 28Volt) per Remote Unit or I.A., and 5 Watt for the DRU.

Small size: Dimensions for typical configurations are shown in Figure 2..

Mass: 5 lb per RU, 6 to 9 lb per I.A. and 5 lb for the DRU.

There is no cable length limit for an orbiter mission.

The sensors are fully protected inside the sensor/signal conditioning units.

If desired, a small, sensors-only box can be housed in a very small package (see Fig.2) and located inside an experiment unit, close to the samples for instance.

Highly flexible multiwire ribbon cables are used to connect Remote Units with the DRU.

COST: A very low cost approach was maintained for the development and applies to all operations in accordance with the commercialization of space objectives.

POST MISSION DATA DISSEMINATION:

Post mission, all the raw measured data is transferred to CD ROM and is available to P.I.'s via Internet or otherwise. In addition, data can be processed for microgravity disturbing components, such as frequencies, average levels and transient levels and the low rate reduced data made available.

PANORAMIC DATA DISPLAY:

For the analysis of data and convenient presentation, a novel "panoramic" data display method was developed showing simultaneously the responses measured in the three frequency bands and at the several Remote Unit locations for e.g. 10 minute periods See Fig . A complete shuttle mission can be browsed in less than an hour to find the salient and relevant disturbances.

3-DMA DEVELOPMENT TEAM:

The 3-DMA Team involved in the initiation and development of the 3-DMA one time or another included the following:

Jan A. Bijvoet, Program Director / Principal Investigator
Philip D. Nerren, System Integration and Data Processing
Jeffrey A. Randorf, TSD Consultants: Invertable Accelerometer
Craig P. Schafer, Electronics
John R. Blakely, Noval Data Display
Lauritz D. Larsen, Applied Astronautics, PC 104 system and software.
Robert E. Wood, Consultant, Software
Lyle B. Jalbert, Software System aspects
James Currie, Orbital Sciences, Signal Conditioning and Bias Control
John Weber, Orbital Sciences, Signal Conditioning and Telemetry
Gregory Tyler, Stephen Collins, Machining
Ken Barton, Vernon Mullins, Consultants, PC Boards design
Jesse Hipps, Consultant, 3DMA / ARIS Software.
Chakravarthy Deverapalli, I.A. analysis software

Three Dimensional Microgravity Accelerometer

FIG.1: 3-DMA SUPPORTED MISSIONS
Different 3-DMA configurations

SPACE SHUTTLE

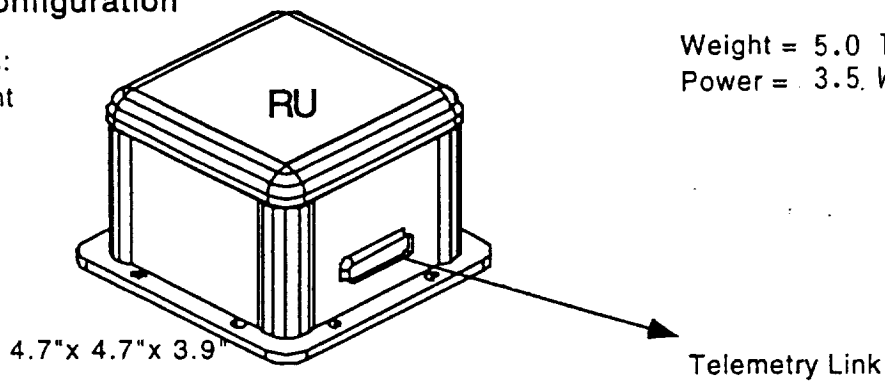
- CONCAP III,TETHER, STS-46, 8/92	CONSORT 1,2,3	'89 - '90
- SPACEHAB 01,	JOUST	' 91
- SPACEHAB 02,	CONSORT 4,5,6	'91 - '93
- SPACEHAB 03,	METEOR	10 / 95
- Spacelab, USML 02, STS 73, 10/95	CONQUEST - 1	4 / 96
- SPACEHAB 05, ETTF, MACEK & ARIS, STS 79, 8/96		
- SPACEHAB-SM	STS 95, 11/98	

FIG.2: Typical 3DMA Flight Configurations

Smallest Configuration

Mounted on:

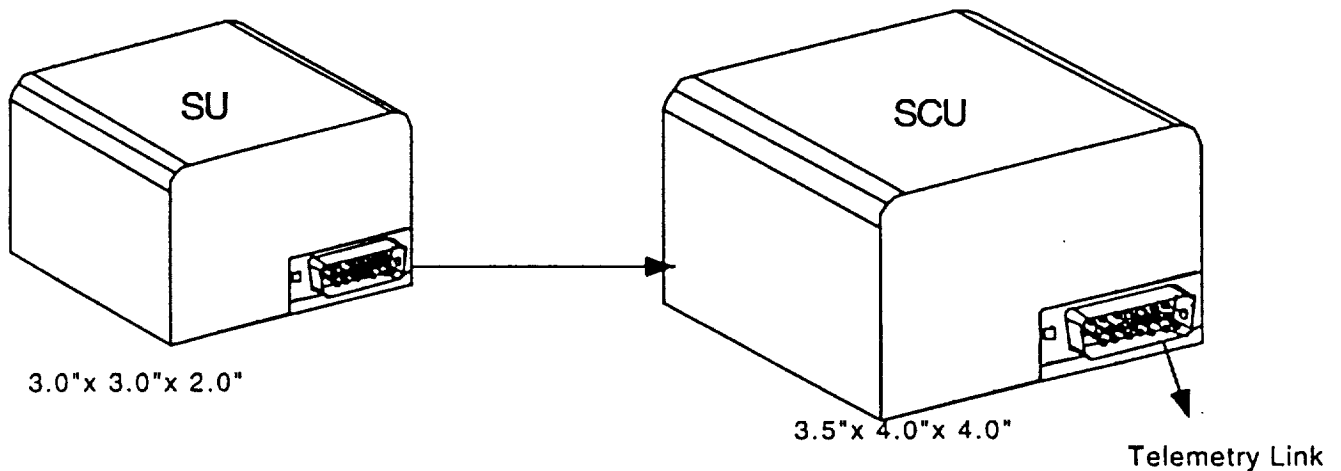
- Experiment
- Rack
- Bulkhead



Weight = 5.0 lbs
Power = 3.5 W @28V

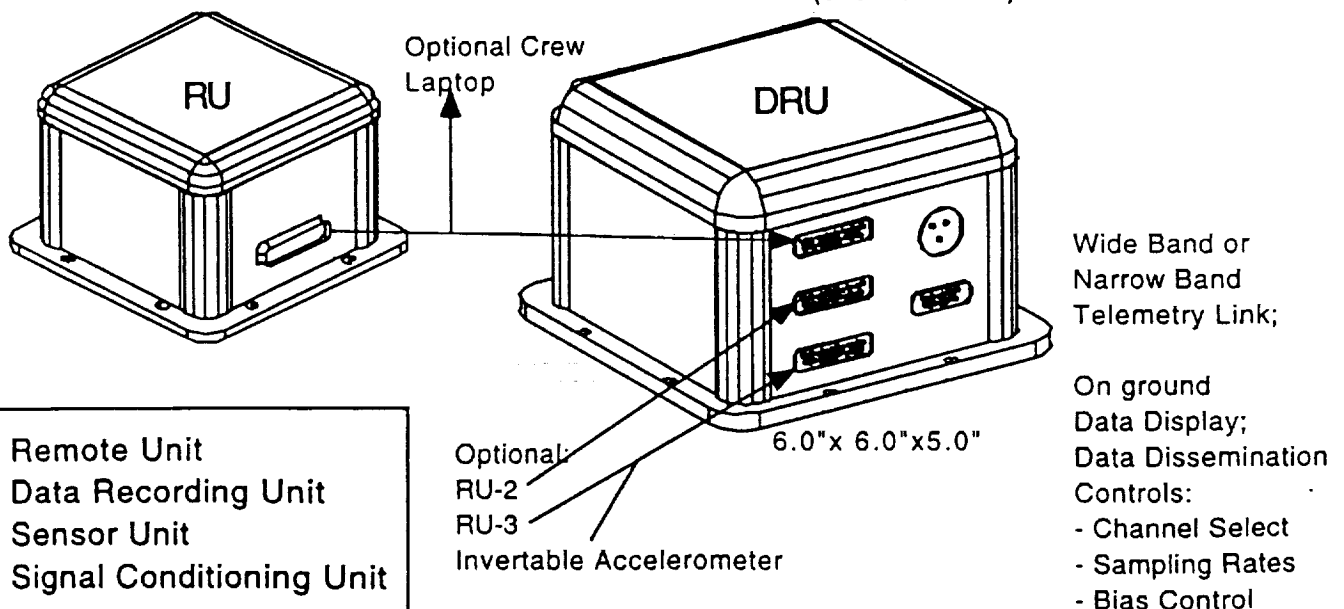
Sensor Internal to Experiment

Weight = 7.0 lbs. total
Power = 3.5 W @28V total



Sensor External to Experiment w/Data Recording

Weight = 10.0 lbs.
Power = 8.5 W @28V
(one RU + DRU)



RU = Remote Unit
DRU = Data Recording Unit
SU = Sensor Unit
SCU = Signal Conditioning Unit

The University of Alabama in Huntsville

Attn: Mr. J. Bijvoet

301 Sparkman Drive NW

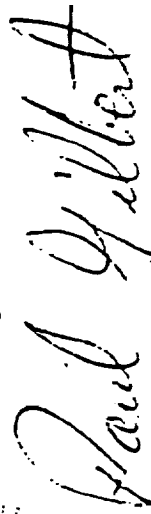
Consortium for Materials Development In Space

Huntsville, AL 35805

Dear Mr. Bijvoet:

On behalf of the mission team at Marshall Space Flight Center, I would like to congratulate you and your 3DMA team on the successful performance of your experiment on USML-2. USML-2 has been called our most trouble free module mission. Clearly, the dedicated efforts of your team in constructing and operating your experiment contributed to this success. The use of your real-time acceleration data, in conjunction with the operation of the Surface Tension Driven Convection Experiment, demonstrated the need for this type of operation on future flights. We look forward to seeing the final results of your acceleration measurements.

Sincerely,



Paul Gilbert

USML-2 Mission Manager

FIG.3: STATEMENT USML)@ MISSION MANAGER

cc:

HQ/USM/Mr. McGuire

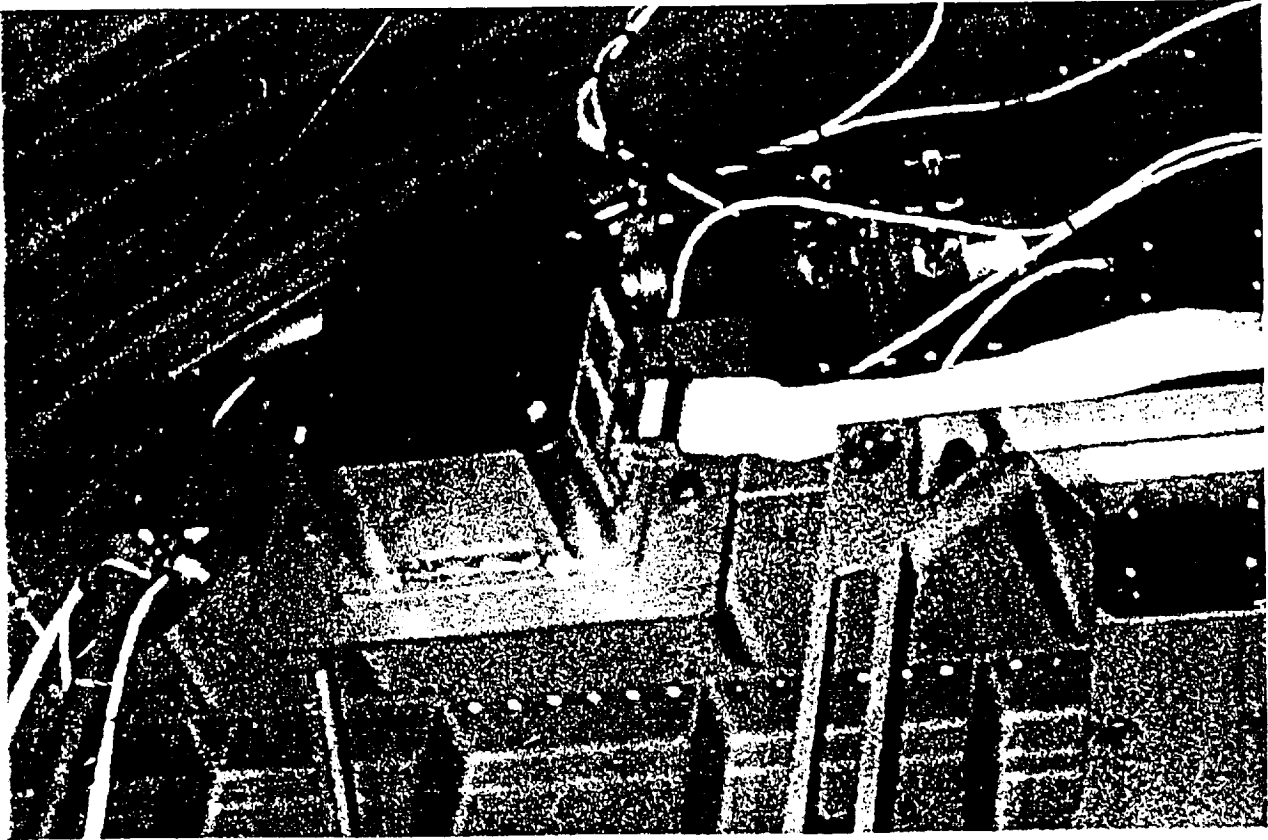
HQ/XP/Dr. Ambrus

FIG. 4: 3 - DMA TECHNOLOGIES VALIDATED

- 3 SIMULTANEOUS FREQUENCY BANDS EACH ACCELEROMETER
- HARD DISK DRIVE VIABILITY
- FULLY AUTOMATIC DATA RECORDING
- TRUE REAL-TIME ACCELERATION DATA TO GROUND (USML-02)
- INVERTABLE ACCELEROMETER
- HIGH - G ASCENT & μ G ON ORBIT WITH SAME INSTRUMENT
- "FREE-FLYER" PC-104 DATA PROCESSOR (CONQUEST 4 / 96)
- NO SUPPRESSION OF "DC" COMPONENT
- VERY LOW NOISE LEVEL
- SENSITIVITY INCREASE & BIAS CONTROL
- NOVEL PANORAMIC DATA DISPLAY
- PRE-MISSION μ G MISSION SEQUENCE TEST

**3-DMA
REMOTE UNIT
ON
AFT BULKHEAD
SPACEHAB
STS-95**

FIG. 5.



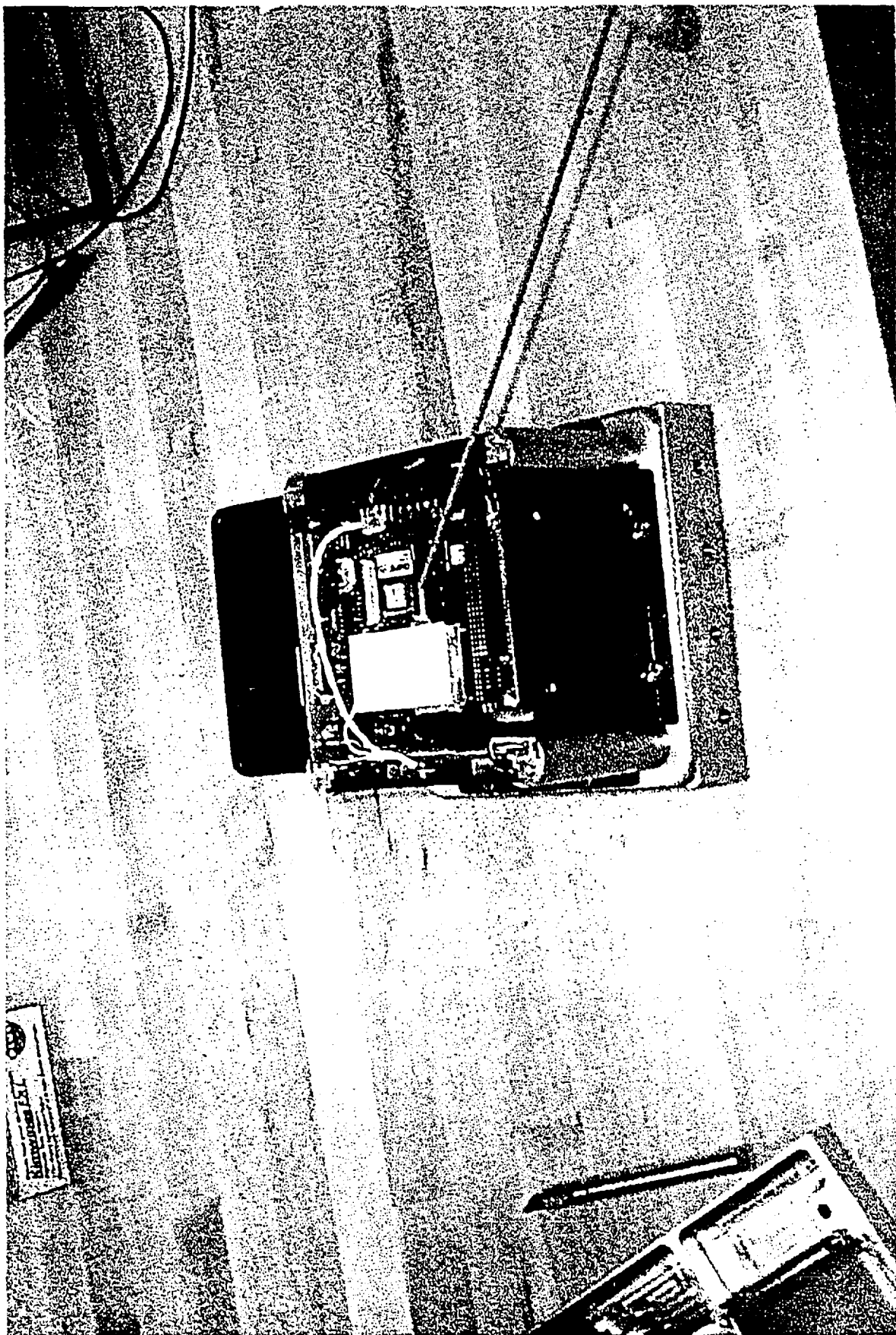


FIG. 6: DATA RECORDING UNIT (DRU)
Lid removed to show location clock battery

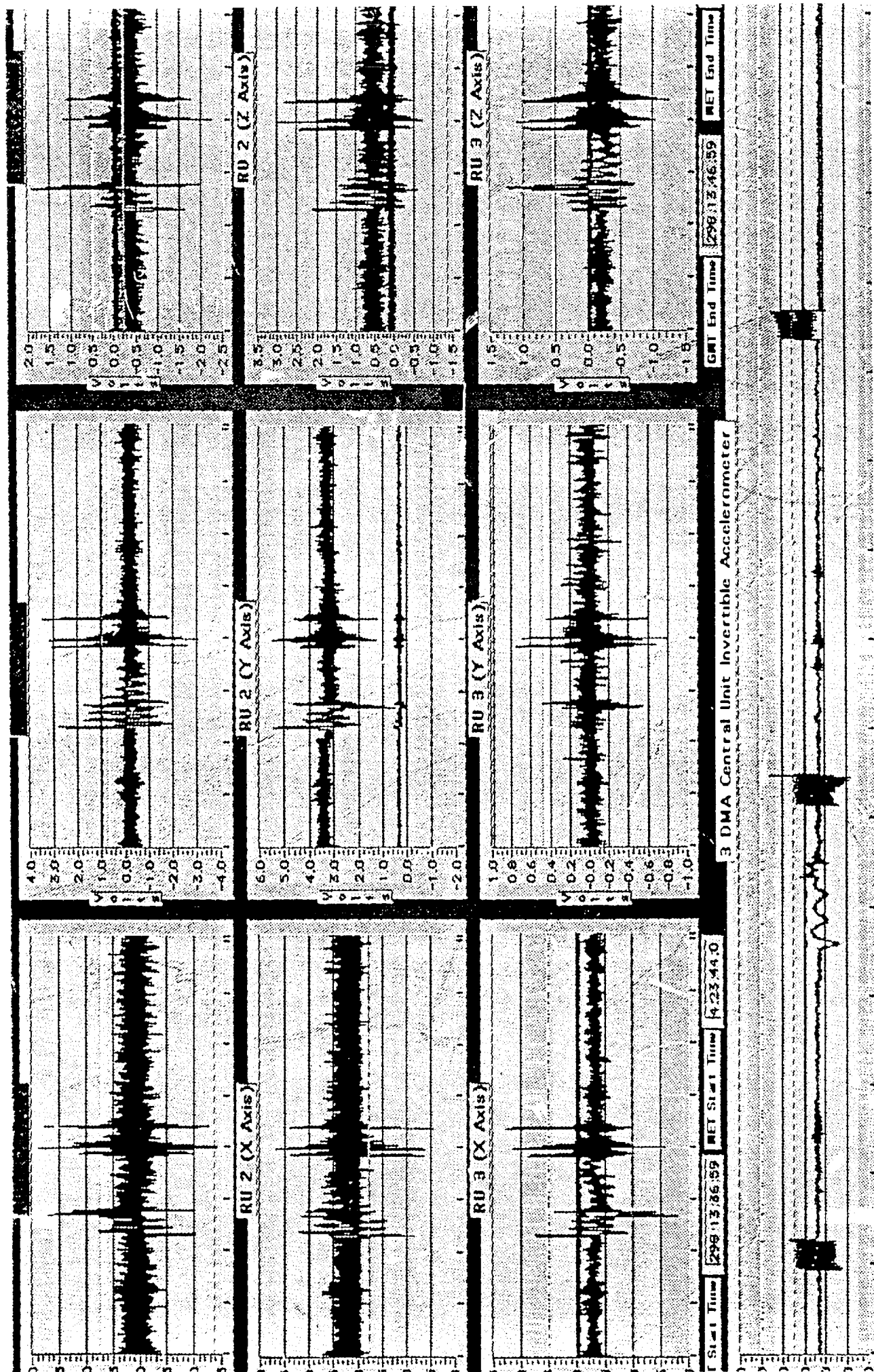


Fig. 7: EXAMPLE OF PANORAMIC DISPLAY.
Data from STS 60, SPACEHAB 02, February 1994

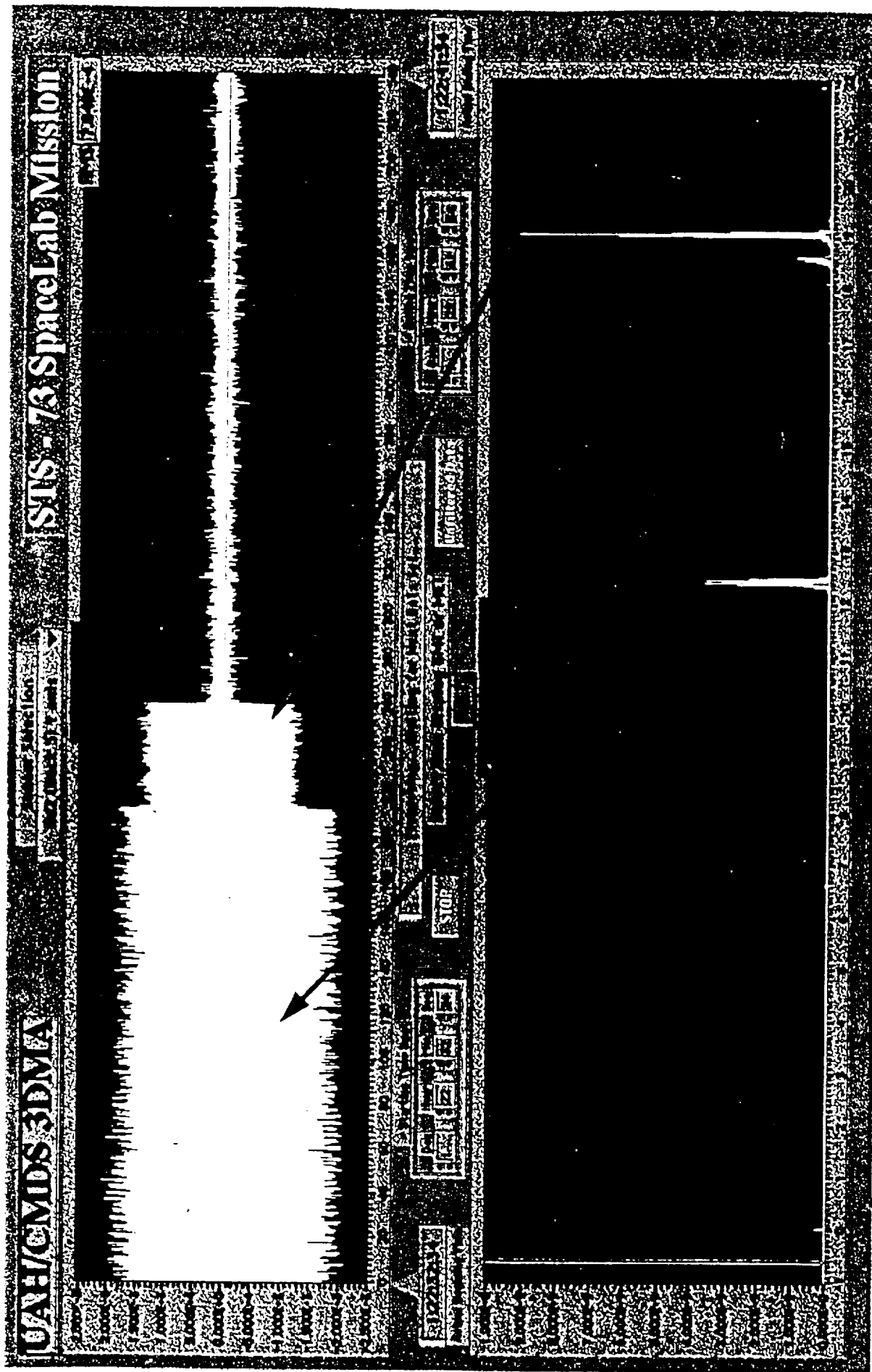


Figure 8 . Glove Box Fan Turned Off In 2 Steps

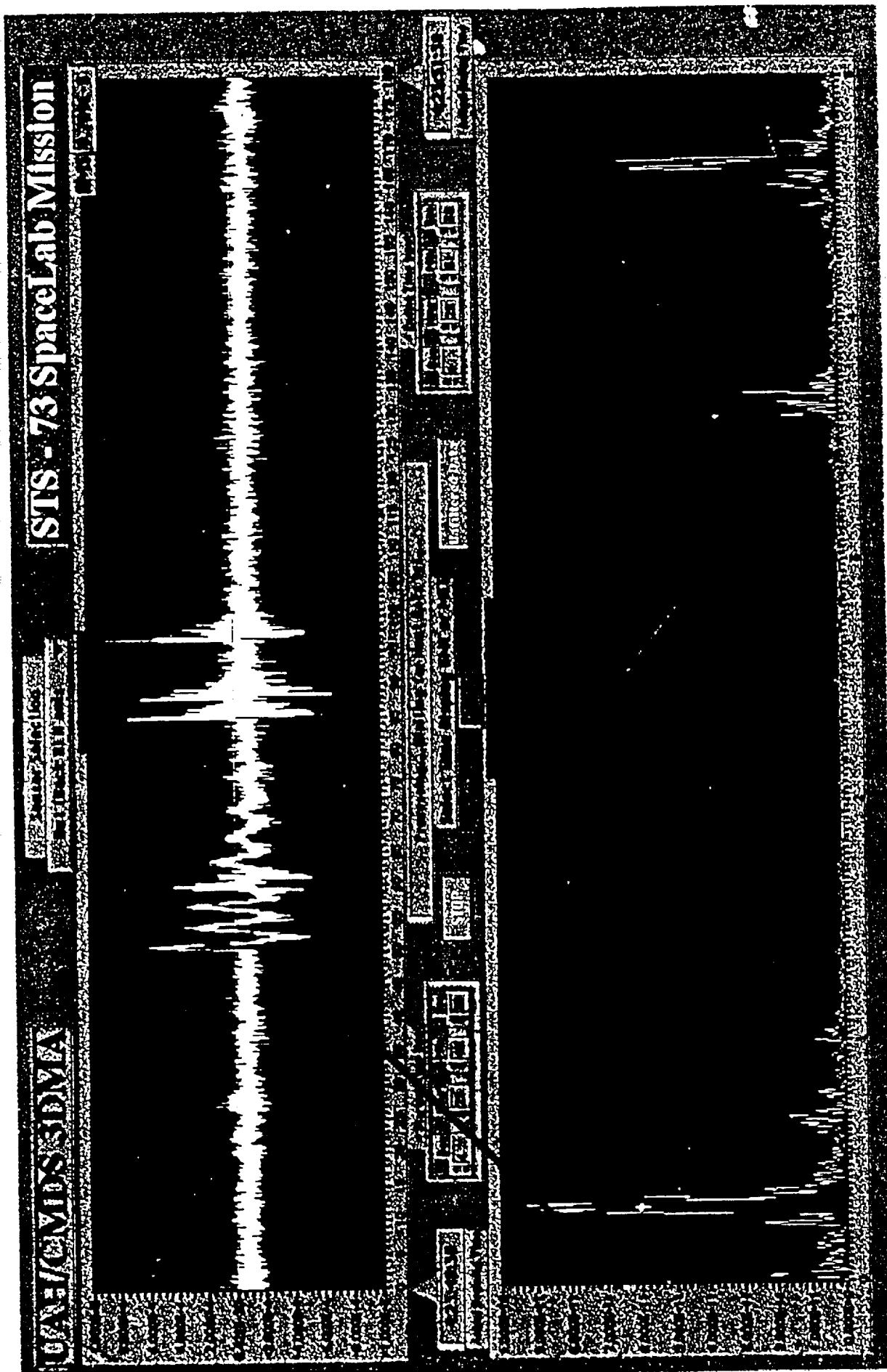


Figure 9 . Payload Bay Door Opening (0-5 Hz spectrum)

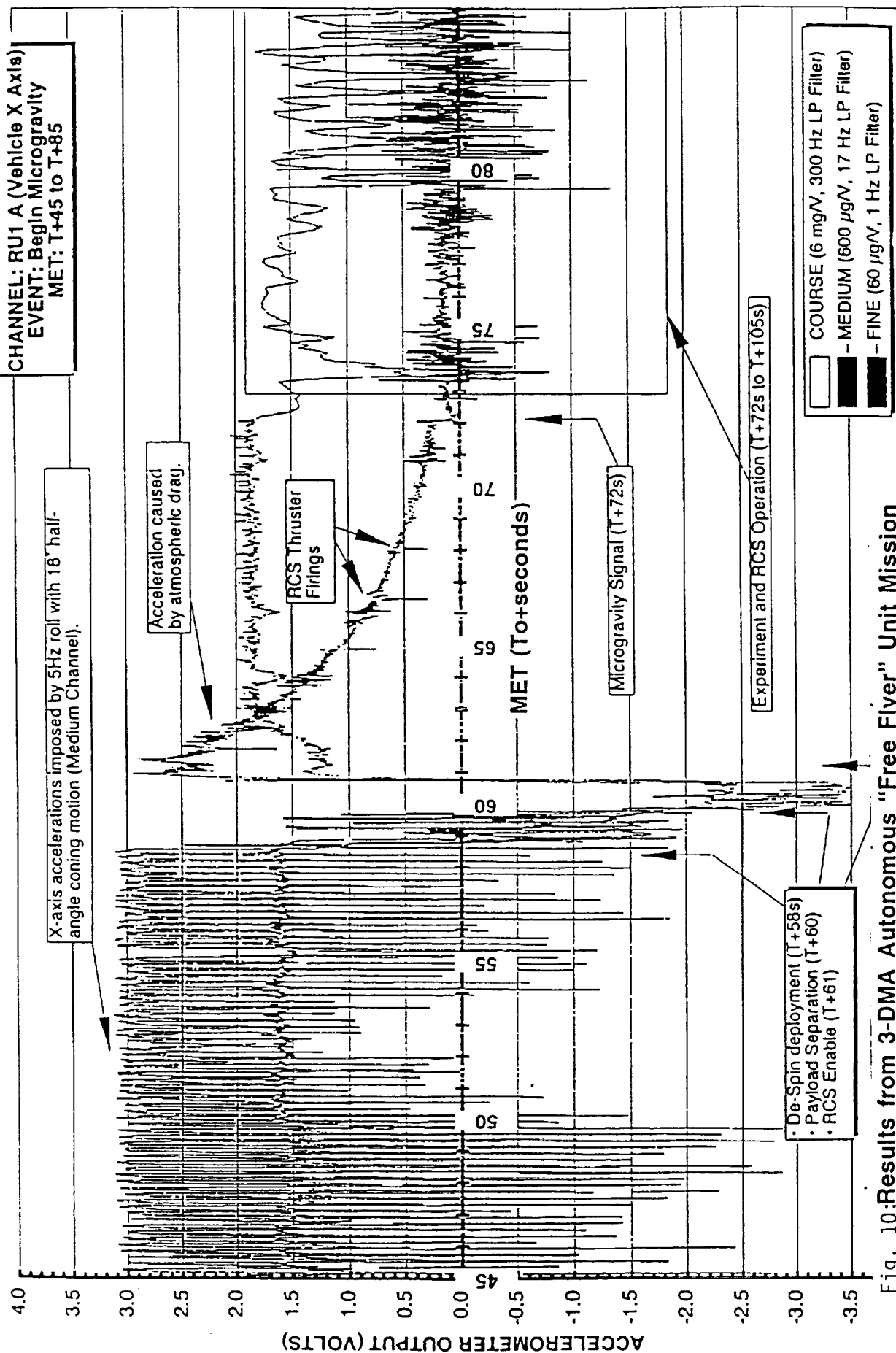


Fig. 10: Results from 3-DMA Autonomous "Free Flyer" Unit Mission on CONQUEST 1 Sounding Rocket Mission, April 1996.

Leaving Earth Atmosphere is detected by the gradual drag decrease shown after De-Spin and Payload Separation. (Maximum at 61 seconds is 1.6 milli-g drag)

After 80 seconds disturbances are registered from initial experiment fluid stirring operations ("GOSAMR" Experiment).

CONQUEST I - 3APR96
3DMA DATA

CHANNEL: RU1 C
EVENT: Early Microgravity
MET: T+85 to T+125

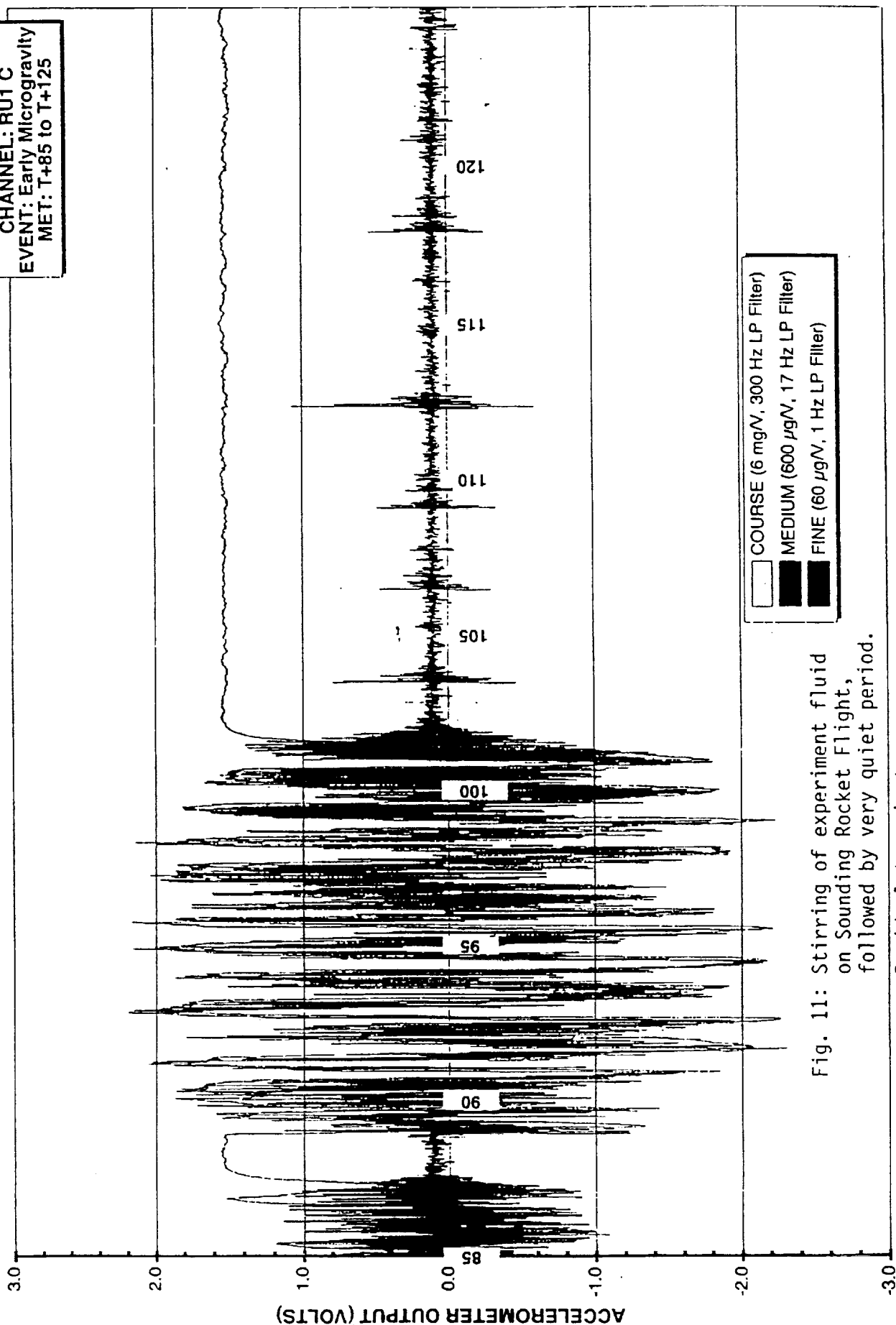
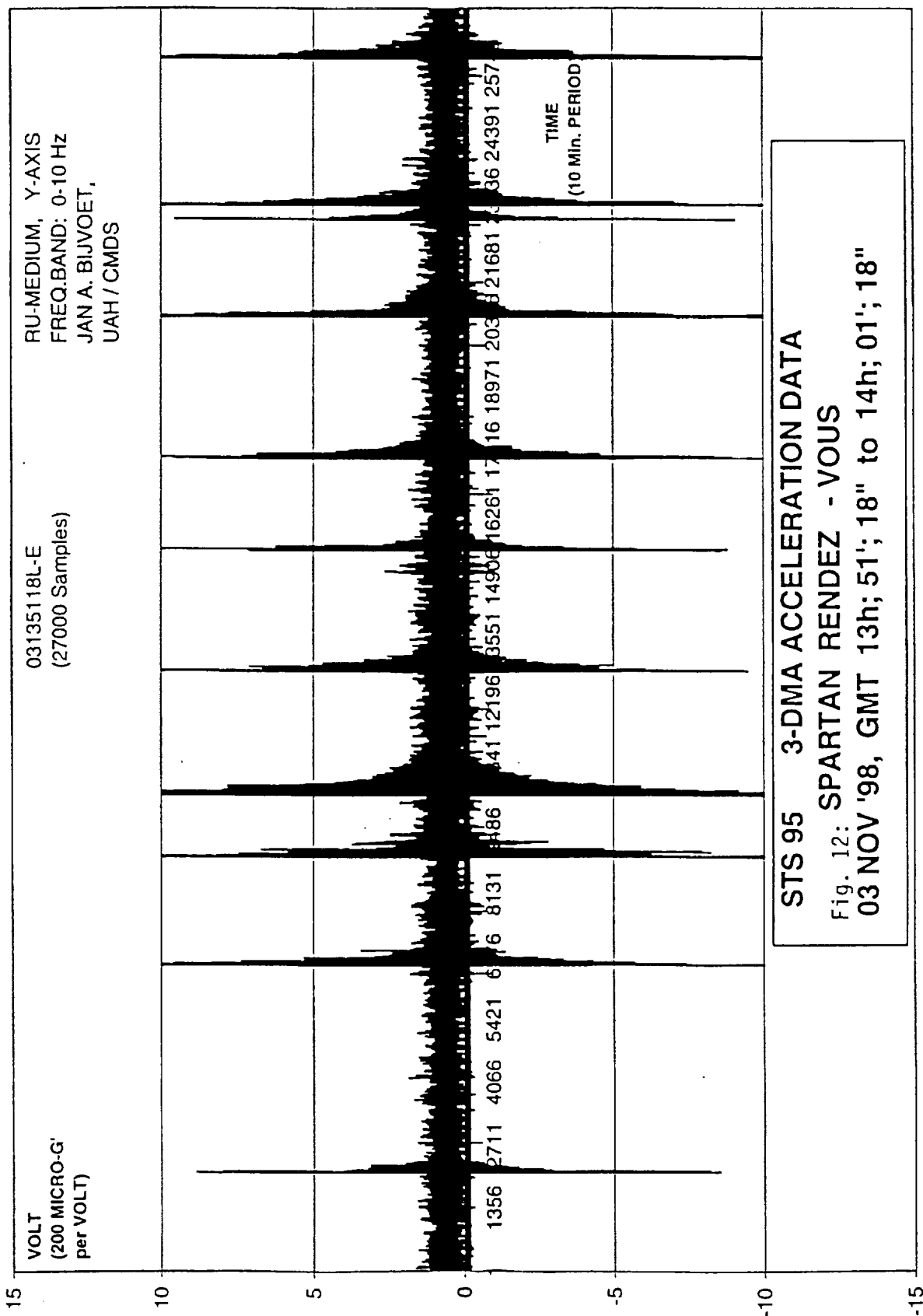
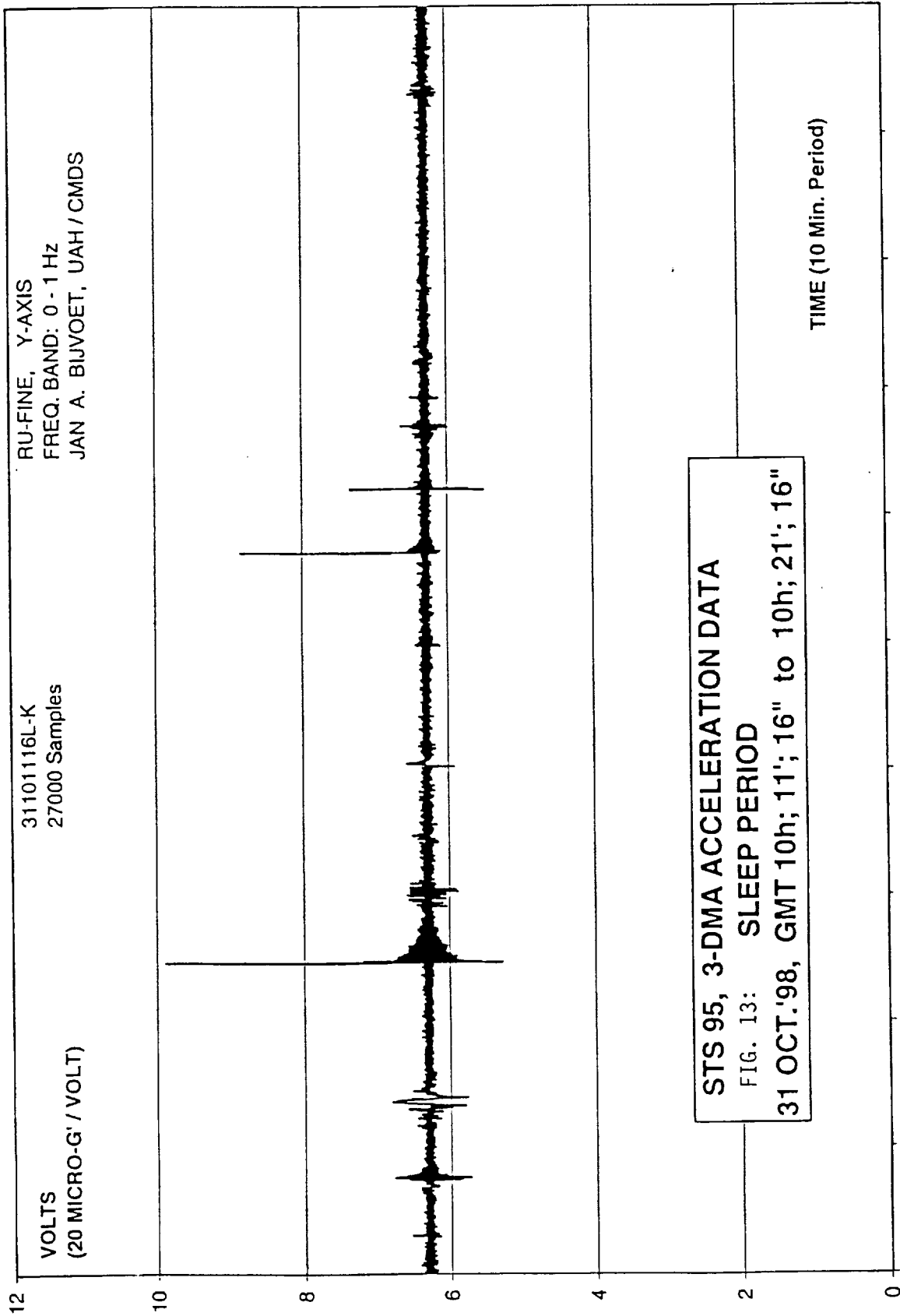


Fig. 11: Stirring of experiment fluid
on Sounding Rocket Flight,
followed by very quiet period.

Residual transients
are caused by opera-
ting photo camera's.

MET (T+seconds)





1 1353 2705 4057 5409 6761 8113 9465 10817 12169 13521 14873 16225 17577 18929 20281 21633 22985 24337 25689

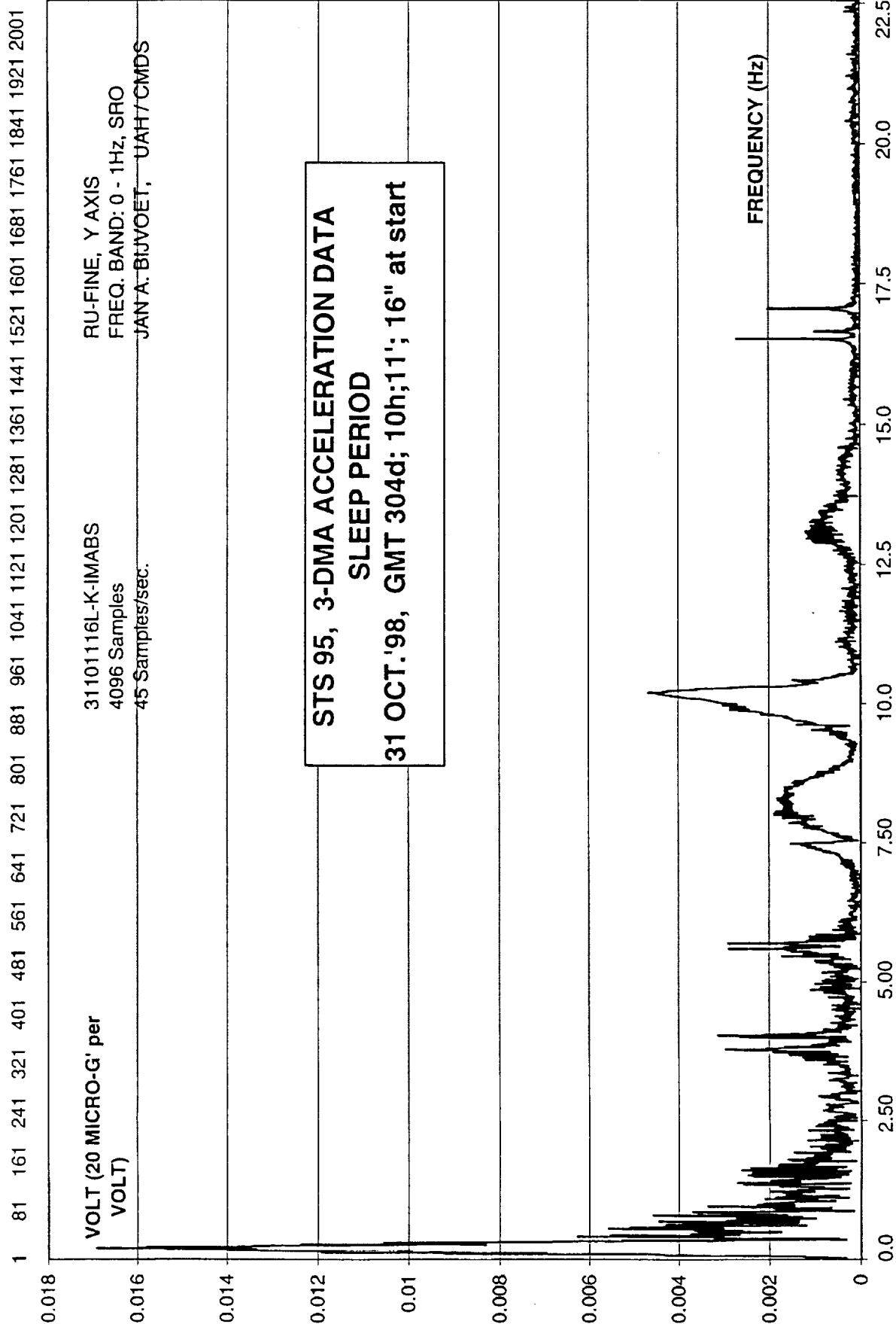
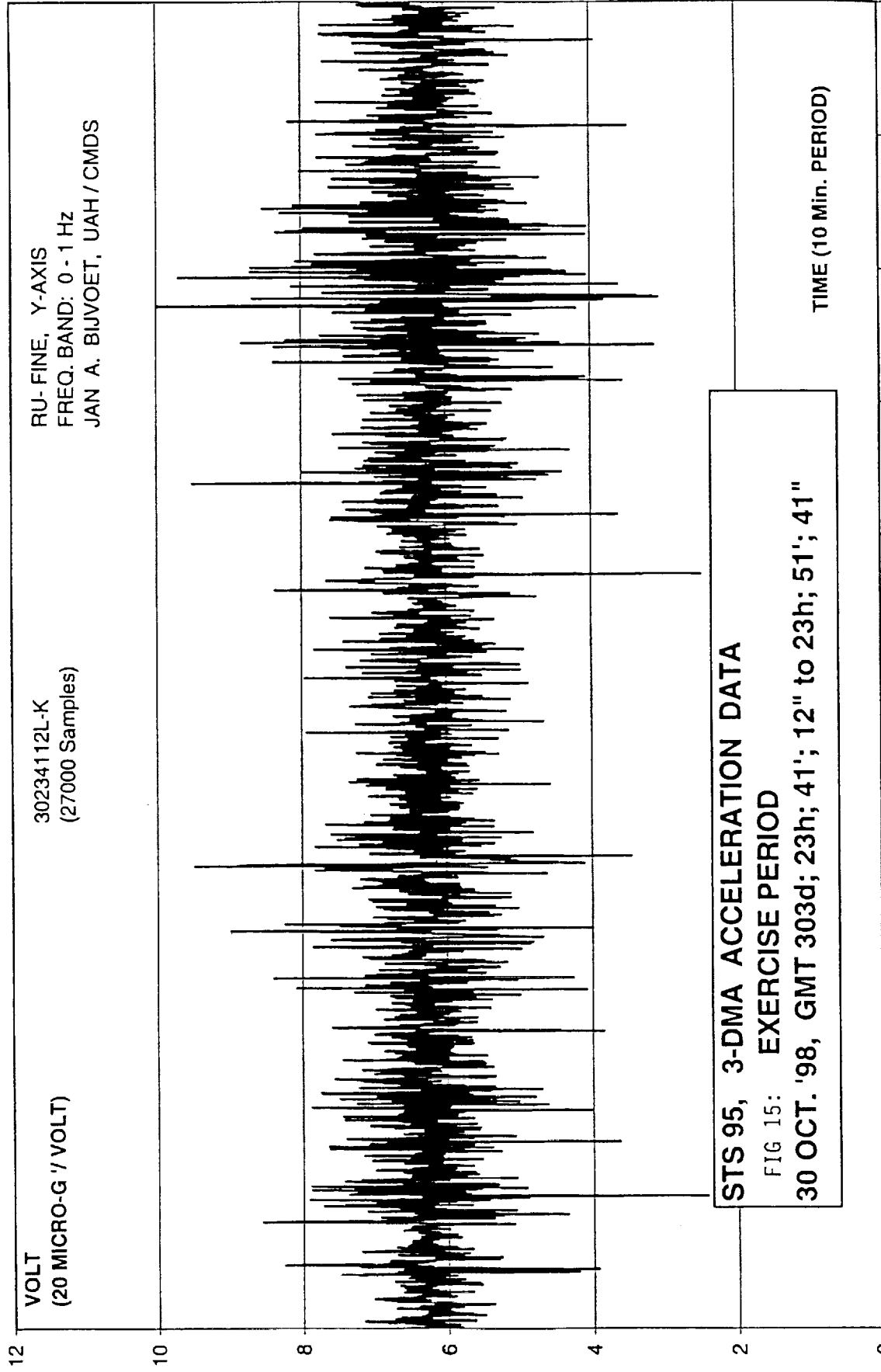


FIG. 14: FREQUENCY SPECTRUM FOR SLEEP PERIOD,
FINE CHANNEL

CHART 3



1 1289 2577 3865 5153 6441 7729 9017 10305 11593 12881 14169 15457 16745 18033 19321 20609 21897 23185 24473 25761

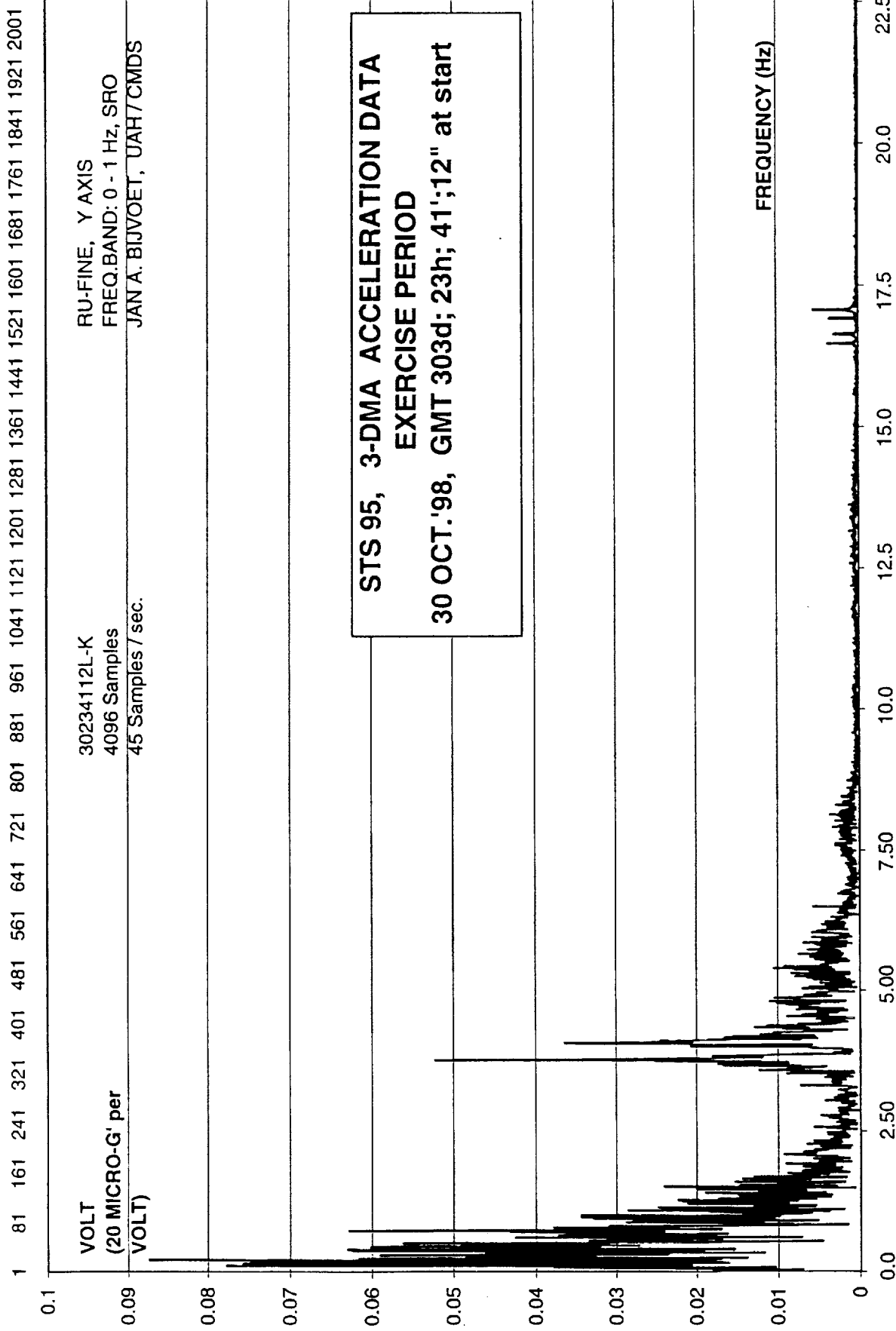


FIG 16: FREQUENCY SPECTRUM FOR EXERCISE PERIOD; FINE CHANNEL

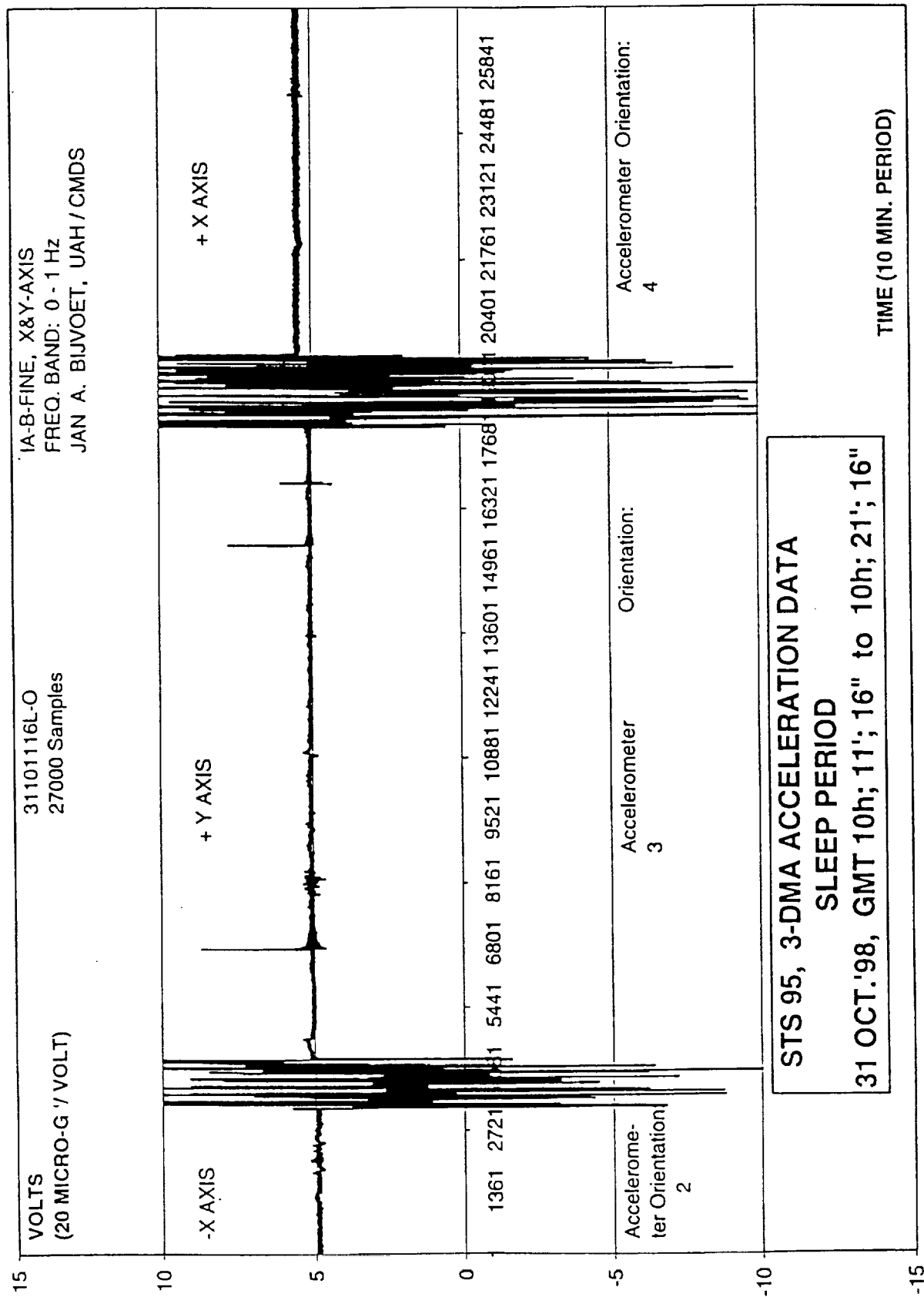


FIG 17 & 18: INVERTABLE ACCELEROMETER DATA.

The shift in average acceleration level from + X axis to - X axis shows the detection of absolute - G in the X direction. Similarly for the Y direction.

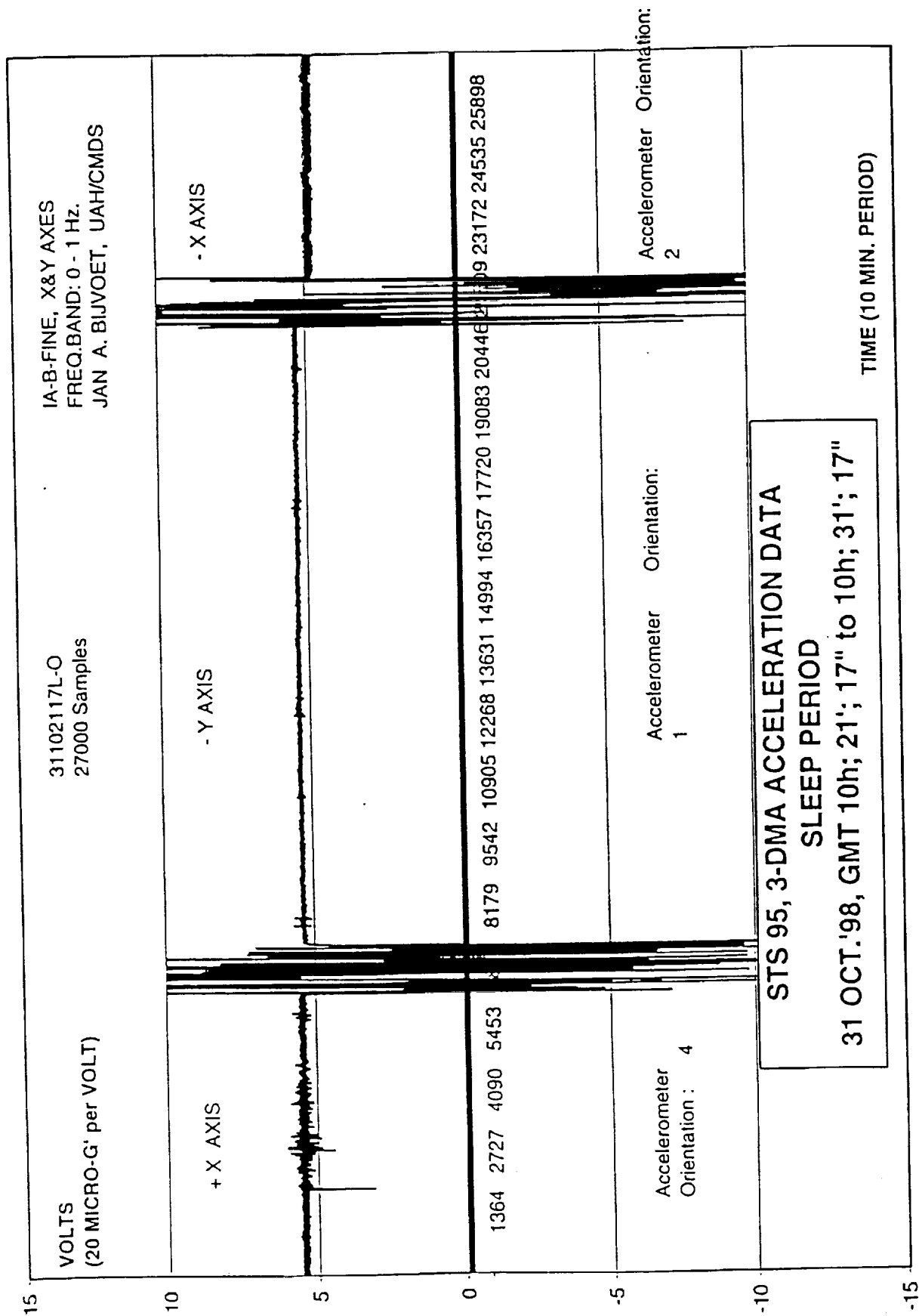


FIG 18: See text with Fig. 17.

APPENDIX B

BioDyn Final Report

FINAL REPORT

The University of Alabama in Huntsville BioDyn Project



Project Manager
Marian L. Lewis, Ph.D.

Consortium for Materials Development in Space



University of Alabama in Huntsville

IN APPRECIATION

The BioDyn Project could not have been possible without the vision, direction, and management of Dr. Charles A. Lundquist, Director of the UAH Consortium for Materials Development in Space 1985-1999. His goal-oriented leadership both encouraged and energized those whose good fortune it was to work with him. His support of creativity gave us the freedom that resulted in accomplishing, not only the goals of the program, but also those achievements contributing to a larger view of the possibilities inherent in space exploration.

Acknowledgements

The UAH BioDyn team expresses sincere appreciation to the Crew of STS-80. The dedication and attention of Kent Rominger and Story Musgrave to the details of the BioDyn Payload's experiments were exceptional.

Very special appreciation is expressed to the Crew of STS 95. We are sincerely grateful to Astronaut John Glenn, BioDyn's prime crewmember, for the success of the BioDyn Payload. Post-flight analyses showed that every experiment was 100% successful, all science objectives were met, and hardware was operated as desired. To Scott Parazynski, we express our appreciation for his role in conduct of on-orbit BioDyn operations. For her interest in BioDyn's biomedical experiments and enthusiastic involvement in optimizing experiment conditions, we thank Chiaki Mukai. To Steve Robinson we express our appreciation for his interest in BioDyn's experiments and to Commander Curt Brown, thank you for a perfect mission.

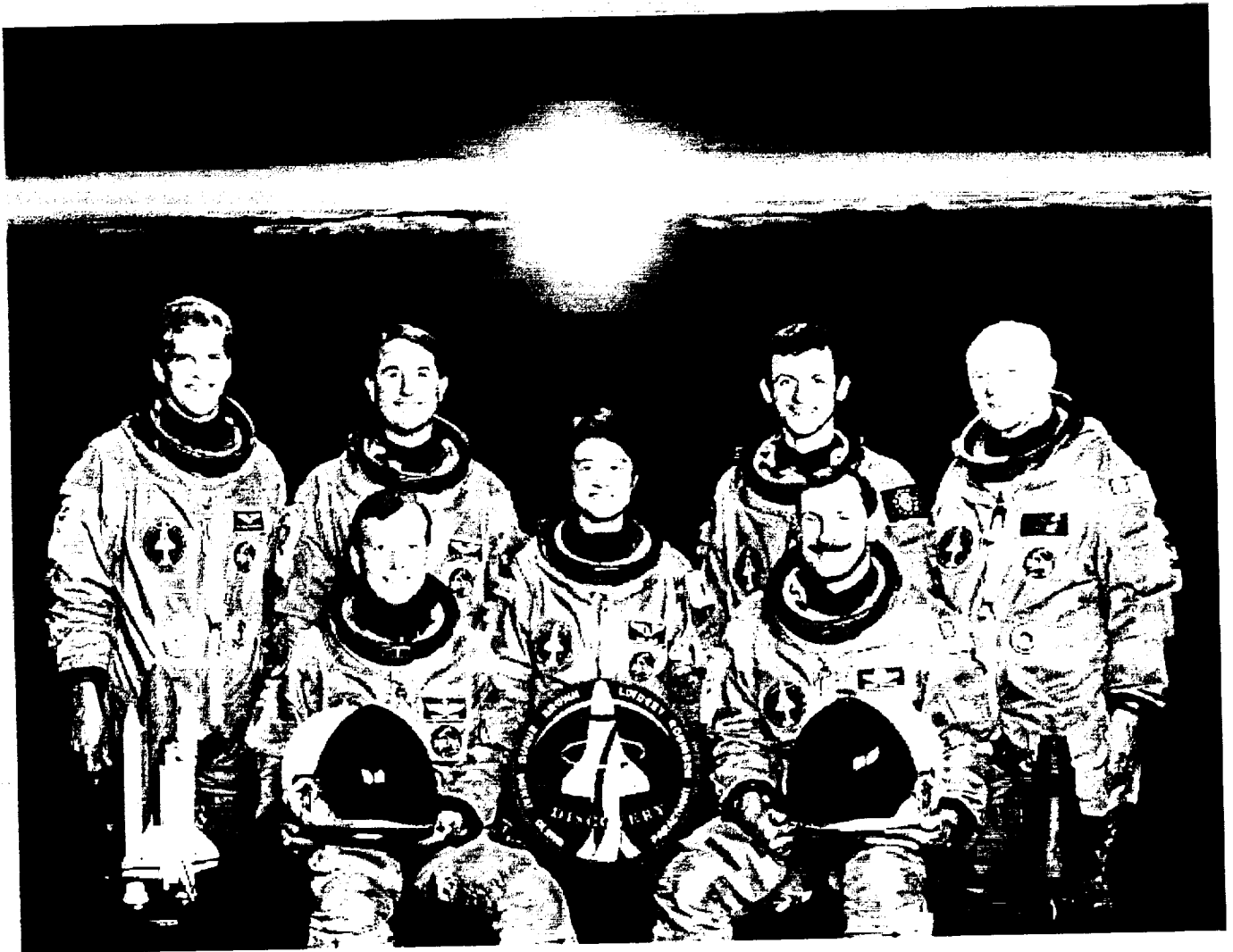
A special acknowledgement is granted to Niki Myers, UAH Mission Manager for the STS-95 BioDyn Payload. Niki's dedication, perception, understanding and performance of the multiple tasks of a mission manager were exceptional. As BioDyn Project Manager, I express my sincere appreciation to Niki for her part in making this mission 100% successful.

Lastly, we express gratitude to BioDyn's industry affiliates for involvement in this pioneering commercial space project. Without their considerable in kind support these commercial experiments, identifying benefits of space processing and products development, could have been performed.

STS-95 Crew Patch



STS-95



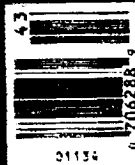
Seated are astronauts Curtis L. Brown Jr. (right), mission commander; and Steven W. Lindsey, pilot. Standing, from the left, are Scott F. Parazynski and Stephen K. Robinson, both mission specialists; Chiaki Mukai, payload specialist representing Japan's National Space Development Agency (NASDA); Pedro Duque, mission specialist representing the European Space Agency (ESA); and U.S. Sen. John H. Glenn Jr., payload specialist.

GAYS AND HATE CRIMES · ALANIS MORISSETTE RETURNS

Newsweek

A New Mission for
John Glenn:
Exploring the
Science of
Growing
Old

BACK INTO
SPACE



John Glenn conducted the STS-95 BioDyn Payload operations in space.

BIODYN
(BioDynamics and Space Cell Culture)

FINAL REPORT

8/31/99

Submitted by
Marian L Lewis, Ph.D., Project Manager

BIODYN PROJECT BACKGROUND

With the primary objectives designed to foster use of the microgravity environment for commercial production of bio-materials from cells, and to develop services and processes for obtaining these materials through space processing, the BioDyn program was initiated with the flight of the first payload on STS-80 in 1996. The program, managed by the University of Alabama in Huntsville (UAH) Consortium for Materials Development in Space (CMDS), was sponsored by NASA's Office of Space Access and Technology, Space Processing Division. Though this payload was flown on only two missions, STS-80 and STS-95, it significantly advanced the potential for commercialization of space in the areas of tissue engineering and products from cells cultured in microgravity.

BioDyn evolved from the activities of the UAH CMDS Materials Dispersion and Biodynamics Program (1992-1996) of which the Commercial MDA ITA Experiments (CMIX) constituted the primary payload. From experience and data derived from the UAH experiments flown on CMIX under joint agreements between UAH and NASA and UAH and Instrumentation Technology Associates, Inc. (ITA) of Exton, PA, the commercial biomedical target products for the UAH BioDyn program were identified. Early Shuttle flights of CMIX (STS-52 and STS-56) achieved significant information on cell growth, response and metabolism in microgravity (See appended list of publications). Information from STS-67 and STS-69, flown in 1995, was essential for selection of the commercial biomedical products flown on BioDyn. The experiments flown on STS-80 and STS-95 by BioDyn's industry affiliates and associated university investigators, advanced commercial potential for a number of products. These included multi-layered, aligned heart cells (not achieved by Earth-based culture) with potential for implantation therapy, cellular aging proteins, natural product insecticides from bacteria, anti-cancer compounds produced by plant cells, and superior micro-capsules for encapsulating pancreatic cells for use in treating diabetes. Additionally, significant information gained on cellular response to drugs and drug metabolism advanced the potential for pharmaceutical development in microgravity.

This report describes the commercial products and experiments flown on the 100% successful STS-95 BioDyn Payload.

OVERVIEW OF THE STS-95 BIODYN PAYLOAD

STS-95 was launched on October 29 and landed on November 7, 1998. The goal of the STS-95 BioDyn Payload was to foster the commercial development of space through production of economically important bio-materials by living cells. BioDyn's industry affiliates and commercial products were carefully selected based on a set of rigorously applied, NASA-defined, commercial selection criteria (Appendix I, VG #4). These experiments were pioneer commercial ventures designed to capitalize on the unique attributes of the microgravity environment leading to production of new and improved bio-materials and processes. Products were selected based on relevance to medical conditions of aging such as heart and vascular disease, bone degeneration, and cancer (Appendix 1, VG #2). The experiments included tissue engineering (bone implants and heart muscle patches), factors produced by cells to control cancer cell growth and aging at the cellular level, and plant cells producing anti-cancer and anti-alcoholism compounds. All of these biomedical products have significant humanitarian value and our marketing research showed that these products occupy an existing Earth-based commercial market niche estimated to be in the multiple billions of dollars.

Commercial Space Products: Commercial companies flying experiments on the STS-95 BioDyn Payload (Appendix 1, VG # 3) included; Hauser Chemical, a Colorado company, developing anti-cancer compounds derived from soybean cells in culture; Millenium Biologix, Inc., a Canadian company, with US affiliates, developing implantable tissue engineered bone on artificial scaffolds, and SYNTHETCON, Inc. of Houston, Texas specializing in products from cultured cells including proteins to prevent host versus graft rejection and aging factors. In addition to these companies, the University of South Carolina working to gain information preliminary to entering into commercial agreements with tissue engineering companies, achieved a significant breakthrough in heart cell tissue engineering on the STS-95 BioDyn Payload. **This experiment proved that cell culture in the microgravity environment promotes the tissue assembly process.** Multi-layered, aligned cell patches of heart cells developed in microgravity on artificial substrates. This was not achieved in the ground based process. Heart patches to replace damaged heart muscle could eventually reduce the need for heart transplants thus helping the more than 50,000 people needing a heart transplant each year to survive. Only about 2000 donors are available yearly. STS-95 was the third flight of the heart patch experiment. The objective on STS-95 was to gain further information on the process by which this microgravity-related cell association occurs. This information is critical in the process of developing patents and working with biotechnology companies to produce heart patch implant materials as the technology matures.

Also in the area of tissue engineering, UAH industry affiliate, Millenium Biologix, Inc. flew a bone implant development experiment on STS-95. This company makes human bone implants by seeding Millenium's proprietary artificial scaffold material with human bone cells. In microgravity, three-dimensional tissue matrices appear to form more readily probably because of better cell-to-cell interactions in the absence of gravity-related factors on earth. Millenium Biologix Inc.'s intent is to make revolutionary medical products from synthetic bone. Millenium flew its artificial matrix and human bone cell experiment on STS-95 under an affiliate agreement

with the UAH CMDS. Space-grown bone matrices have potential as dental implants, long bone grafts, and coatings for orthopedic implants such as hip replacements.

On STS-95, Synthecon, which is a privately held biotechnology company in Houston, TX, in collaboration with UAH tested the hypothesis that the microgravity conditions of space could make possible commercial scale production of medically important, complex human proteins that are difficult to produce efficiently on earth. SYNTHECON's pilot studies have shown that human cells cultured in the SYNTHECON Rotary Cell Culture System™ (RCCS), which mimics some aspects of microgravity, produce greatly increased quantities of recombinant proteins on the ground. While SYNTHECON continues its program of innovative hardware design for ground-based applications, it also has a leading role in transforming basic research findings into therapeutically useful products to treat disease. SYNTHECON has initiated an applied research program engaging in collaborations and sponsored research agreements with several medical institutions to promote commercial technology advances. The company's product development driven requirements necessitated the design and fabrication of the BioDyn Bioreactor that flew on STS-95. UAH in collaboration with Space Hardware Optimization Technology, Inc. (SHOT) under an agreement with SYNTHECON, fabricated the BioDyn Bioreactor to meet the industry-driven requirements. The STS-95 experiment tested the hypothesis that the microgravity conditions of space could make possible commercial scale production of medically important, complex human proteins that are difficult to produce efficiently on earth.

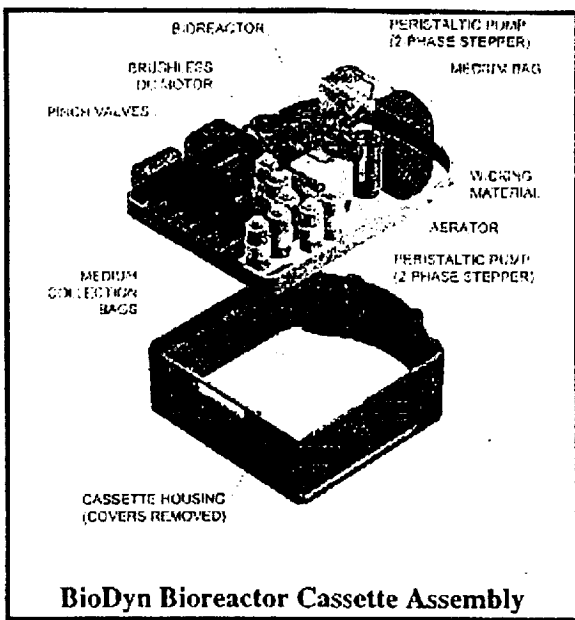
STS-95 BIODYN HARDWARE

BioDyn's experiments on STS-95 were conducted by Astronauts, John Glenn and Scott Parazynski. Three types of hardware were utilized (Appendix I, VG #5). These included 13 Bioprocessing Modules (BPMs), one Automated Bioprocessing Module (ABPM) and the BioDyn Bioreactor operated in the ADSEP processing facility in the SpaceHab module.

The BioDyn Bioprocessing Modules: Assembled at UAH from off the shelf components (Hamilton, Co.) by the BioDyn Project Manager and flown on six previous CMDS missions, the UAH Bioprocessing Modules (BPMs) were operated manually on STS-95 by Glenn and Parazynski. BPMs consist of four plastic syringes interconnected by Teflon tubing to a four-way valve which was attached to an aluminum tray (Figure 1). They were assembled with two or three levels on containment depending on the materials being flown within each individual BPM. The first level of containment consisted of the syringes/plungers and associated valves and tubing. The second and third levels were FEP Teflon bags heat sealed around each BPM. For the cell aging experiments, addition of filter units in line allowed filtration of cells from the culture medium. This permitted us to evaluate the medium and cells separately for products post-flight. The syringes and valves are operated through the teflon bags. The BPMs were activated by opening appropriate valves and injecting solutions between selected syringes. At prescribed times, samples were fixed by manipulating valves and syringes to inject fixatives. The BPMs were attached by velcro to cloth stowage pouches either velcroed to the middeck wall or placed at 37°C in the Commercial Refrigerator/Incubator Module (CRIM).

The BioDyn Bioreactor (BB): The BB, built to accommodate Synthecon's requirements for large volume (50 ml), dynamic cell culture, was designed to operate in the ADSEP processing facility developed by SHOT, Inc. The system was built by SHOT, Inc. through an agreement with Synthecon, Inc. and based on the cell culture requirements as defined by the UAH CMDS Project Manager. On STS-95, the BB was used to culture genetically engineered CHO cells growing on microcarrier beads and producing a specific human protein product developed by Synthecon. The BB was designed as a prototype, to be functionally verified on STS-95, for automated operation on ISS. The system consisted of a cell growth bioreactor vessel equipped with filters and rotary fluid unions allowing perfusion of culture medium. The system allowed collection of samples at pre-set intervals. In-line pinch valves allowed separation of the vessel from the sample collection and spent medium waste bags. Rotation of the vessel assured gentle mixing of nutrients and cells. The 37°C temperature requirement was achieved via the ADSEP processing facility (PF). (Appendix III: Photo of BB in an ADSEP cassette and ADSEP PF)

BioDyn Bioreactor Cassettes



BioDyn Cassettes are capable of producing a wide variety of cultured cells and transplantable tissues (structurally appropriate, functional cellular aggregates) and products from cells in the form of specific proteins, hormones, and monoclonal antibodies. SHOT, Inc. and Synthecon in collaboration with the Consortium for Materials Development in Space (CMDS) at UAH, developed this cell culturing system to include significant miniaturization and custom component development since few commercially available components would meet the space-flight volume and performance requirements. Although the cassettes were designed to the same dimensions as the ADSEP cassettes to facilitate interchangeability, the internal mechanisms differ greatly. The cassettes will have teleoperation capabilities on ISS using Boeing technology.

Figure 3. The BioDyn Bioreactor (Cassette)

The CRIM: The CRIM, provided to the Commercial Space Centers by NASA through a contract with the University of Alabama in Birmingham, provided the thermal requirements for the BPMs and the ABPM which required 37°C and 6°C. A rectangular box that replaces a standard middeck storage locker in the Orbiter Middeck, the CRIM has three major structural components:

1. The rear plate
2. The experiment chamber, and
3. The external thermal enclosure

The CRIM is cooled and heated with a state-of-the-art Thermal Control System (TCS) which has an operating range of 4°C to 40°C and can maintain the internal volume temperature within 0.5°C of the programmed temperature. The BioDyn Payload was launched unpowered at an ambient temperature of approximately 20°C. On-orbit, during the prescribed experimentation time, the temperature in the CRIM was maintained at 37°C. After the completion of BioDyn experiments, the CRIM temperature was then controlled at 6°C to preserve fixed samples. Approximately 5 days later the unit was powered down 24 hours prior to landing and was returned ambient. (Note: The BPMs for RNA isolation and gene expression studies were stored frozen in a separate unit at -80°C after fixation in space).

STS-95 ON-ORBIT ACTIVITIES

The BioDyn on-orbit activities began on the first day of the mission at approximately four hours after launch. The three BPM stowage pouches located in the CRIM were destowed and velcro-attached at the appropriate location on the middeck wall and the individual BPMs were activated by Glenn. Pouches with mammalian cells in the BPMs were placed back in the CRIM at 37°C and the BPM pouch with the plant cell experiment was velcroed to the Middeck wall at ambient temperature and lighting. The ABPM in the CRIM was activated by simply pushing the button on the exterior housing at launch plus four hours when the CRIM was first opened. Experiments in each BPM were fixed or otherwise terminated at pre-defined times by Glenn or Parazynski according to the experiment design. After termination of each experiment and prior to re-entry, BPMs were re-stowed on pouches and the BioDyn Bioreactor was placed back into the middeck CRIM along with BPM pouches.

The BioDyn Bioreactor (BB) cassette was removed from middeck stowage on the first day and placed into the ADSEP Processing Facility in SpaceHab. The system was activated and the BB operated for the pre-planned 96 hour run. At the end of the experiment, the BB was removed from the ADSEP Processing Facility and stowed in the CRIM at 6°C for the duration of the mission until the CRIM power was turned off 24 hours before landing.

The BioDyn mission activities are summarized by the following sequence of procedural events.

- Power-Up CRIM
- BPM Set-Up
- Activate BPMs
- Activate ABPM
- Activate ADSEP Processing Facility
- BB Transfer to the ADSEP Processing Facility
- Fix BPM Samples according to experiment timelines
- Terminate BB run and place BB in the CRIM
- Prepare Re-entry Configuration and restow BPMs
- Power down CRIM at Landing -24 hrs
- Landing

STS-95 BIODYN EXPERIMENT RESULTS

The STS-95 BioDyn Payload was 100% successful. All of the stated mission objectives were met including verification of the automated cell culture systems (ABPM and BioDyn Bioreactor developed for operation on ISS), on-orbit sample processing, and the science objectives of commercial Tissue Engineering and cell products areas. A list of general mission objectives achieved is given below.

BIODYN PAYLOAD MISSION OBJECTIVES STS-95 POST-FLIGHT ASSESSMENT 11/24/98

1. Mission Success Requirements (For total commercial science)	%ACHIEVED
Experiment hardware (BPM) sample activation and fixation	100%
Experiment hardware (ABPM) activation and fixation	100%
BioDyn (BB) Cassette hardware installed and processed through its timeline	100%
CRIM maintain set temperatures	100%
Experiment deactivation and stowage	100%
Return of payload to PI at KSC within 3 hours after landing	100%

RESULTS: SCIENCE OBJECTIVES AND COMMERCIAL PRODUCTS

A. Verification of Cell Culture Systems

- BioDyn Bioreactor (BB) and Recombinant Protein Product:** The first commercial bioreactor flown in space by a CSC, the BB developed by industry affiliates SHOT, Inc. and Synthecon, Inc. in collaboration with UAH, operated successfully during the mission. Subsequent post-flight analyses by the Synthecon PI indicate that the target recombinant human protein was produced by the cells cultured in the BB thus verifying both operational and scientific success. Based on STS-95 successes, SHOT Inc. is currently promoting future use of the BB on ISS to the NASA/JSC Biotechnology organization and to other potential users.
- Automated Bioprocessing Modules (ABPM):** The flight and ground control APBMs designed and built at UAH, operated successfully during the mission. Analyses of the cells in the UAH Microgravity Biotechnology Laboratory show that the cells were maintained viable until fixed automatically by the device at the pre-set time during the mission. The ABPM will be useful for conduct of a variety of cell culture experiments requiring medium volumes in the range of 10-20 ml and automated capability on ISS and may be expanded to include protein crystal growth experiments.

B. Cell Science Objectives:

1. Tissue Engineering - Heart Patches (University of South Carolina and Industry Affiliates).

The following description of the STS-95 heart patch experiment was provided by the USC PI. "We were once again lucky and the experiments worked as we expected (and hoped) they would". The results that were expected corresponded with those of the Heart Patch Experiments flown on STS-69 and STS-80 shown below.

Figure 4. Heart Patch Experiment.



STS-69- Heart Patch Experiment.

Rat cardiac myocytes were pre-aligned on an artificial substrate before launch. On orbit, the same type of cells suspended in culture medium were added to the pre-aligned cells. After 48 hours in microgravity, cells were fixed by addition of a formalin-based fixative. Post-flight, the actin cytoskeleton was stained in flight and ground controls with rhodamine (red) and membranes of the suspended cells were stained with a green fluorescing dye. In the microgravity samples, the added cells (Green) intercalated into the template and developed into aligned, multi-layered cultures (Lower panel). The suspension cells of the corresponding ground control remained clumped on top of the template layer (Top panel).

The overall objective of the STS-95 experiment was to examine why multilayered, aligned, patches of cardiac myocytes form in microgravity but do not form in ground based tests. As we learned from our previous experiments (Fig. 4 above), when we mix two populations of cells in the ground control, the cells do not interact properly and this results in the initial monolayer of cells with clumps of cells from the second population resting on top of the monolayer. This would not be suitable as implant material. Conversely, when these two cell populations were mixed in microgravity on STS-69 (Figure 5 above) and STS-80, the cells interacted to form a multi-layered, aligned cell culture reminiscent of that seen during normal cardiac development. We hypothesized that this is due to a microgravity-permitted cell-cell signaling mechanism. The multilayered nature of the patch from the STS-95 experiment is shown in Figure 5.

Figure 5. Scanning electron micrograph of aligned, multilayered cardiac myocytes flown on STS-95. (Top panel is the control and bottom panel is flight).

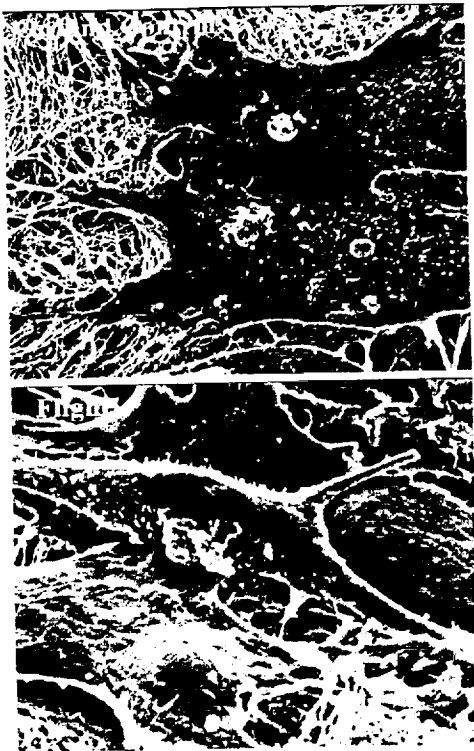
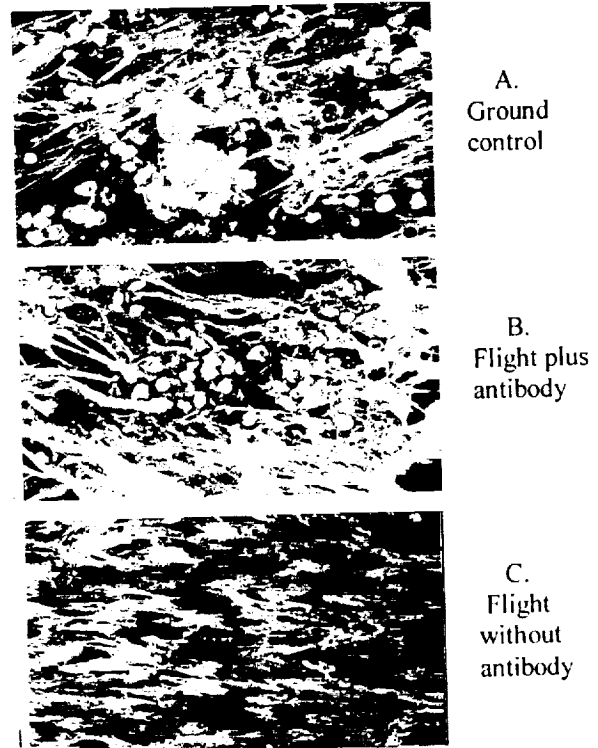


Figure 6. Scanning electron micrograph of cardiac myocytes flown on STS 95 with and without antibody to a specific cell adhesion factor.



The STS-95 experiment showed that the interaction of cells in microgravity could be blocked by adding a specific antibody to a cell-cell signaling factor (Figure 6, B vs. C). The importance of this information is that by identifying the factor operating in microgravity, the same factor can be tested in the ground-based process to enhance the potential for earth-based transplant technology. Conversely, if the process cannot be optimized on the ground, aligned, multilayered heart patches may be produced in microgravity. The STS-95 experiment results indicate that the specific cell-cell signaling pathway important to **normal layering of cells during heart development** is operating in microgravity. This information is important to earth based tissue engineered development of heart patches as a potential way to replace damaged heart muscle suffered by the thousands of heart attack victims each year. This experiment has validated the advantage of the microgravity environment for manufacturing human tissue replacement components. **In the case of tissues which are not easily "built" through tissue engineering on the ground, we have now shown the potential for microgravity processing.**

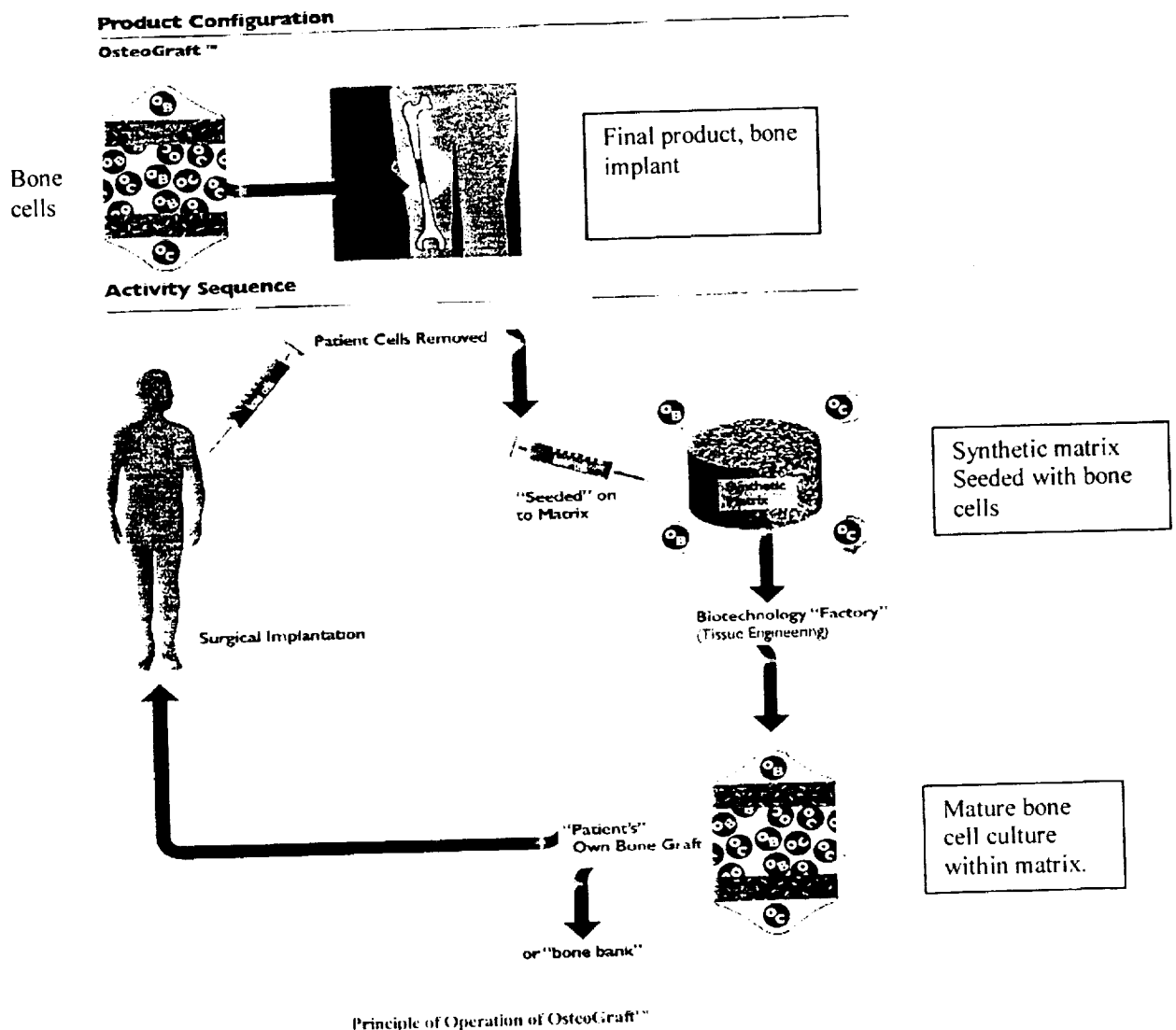
The USC PI expresses appreciation to the NASA commercial program for the opportunity to conduct these commercially important experiments and looks forward to the next opportunity to fly since at this time there are many more questions than answers about the observed cell interactions and potential for commercial production of normal heart muscle suitable for transplantation. Disclosures have been made by the USC PI to two biotechnology companies based on the STS-95 experiment.

It should be noted here that the USC experiments, systematically conducted, and building on the success of three sequential BioDyn experiment missions, have provided the basis for approaching other tissue engineering companies to market microgravity as a means for making commercial human replacement components. The BioDyn Project Manager was recently approached by such a company.

2. Tissue Engineering: Bone Implant Experiment- Millenium Biologix.

The objective of this commercial experiment was to determine feasibility of achieving human osteoblast infiltration and growth in the Millenium Biologix proprietary scaffolding material. Millenium markets the implant material and has plans to make artificial bone implants using human bone cells and the Millenium scaffold (Figure 7).

Figure 7. Millenium Biologix artificial bone implant products.



STS-95 was the first flight of this experiment and the initiation of a UAH industry affiliation with Millenium. The experiment was successful and all objectives were met. The Millenium Biologix PI reports that what was most encouraging was the clear evidence of human osteoblast migration through the interconnected porosity of the Millenium Biologix artificial scaffold material. "Post-flight we could clearly see stained 'healthy' looking cells everywhere". Overall, Millenium was very encouraged by the results which, despite the short experiment duration and non-optimized temperature because of lack of ascent and descent power to the BioDyn Payload on STS-95, have shown that these synthetic bone biomaterial substrates and bone graft scaffolds support human osteoblast functioning. The Millenium PI states that **"This is a good start from which to design further, more quantitative experiments"**.

3. Protein Products from Cells: UAH Cell Aging Factor Experiment (Industry Affiliate, Synthecon, Inc.)

The purpose of this experiment was to confirm the microgravity-related, time-dependent appearance of a cell death factor noted on previous flights. This type of factor is being used commercially as a treatment for cancer. A protein, on the surface of actively growing malignant lymphocytes, targets them for reaction with this soluble cell death factor and initiates a cascade of events leading to death of the cell. Cell samples from microgravity experiments, clearly show that cancer cell aging and death in microgravity are different from ground (Figure 8).

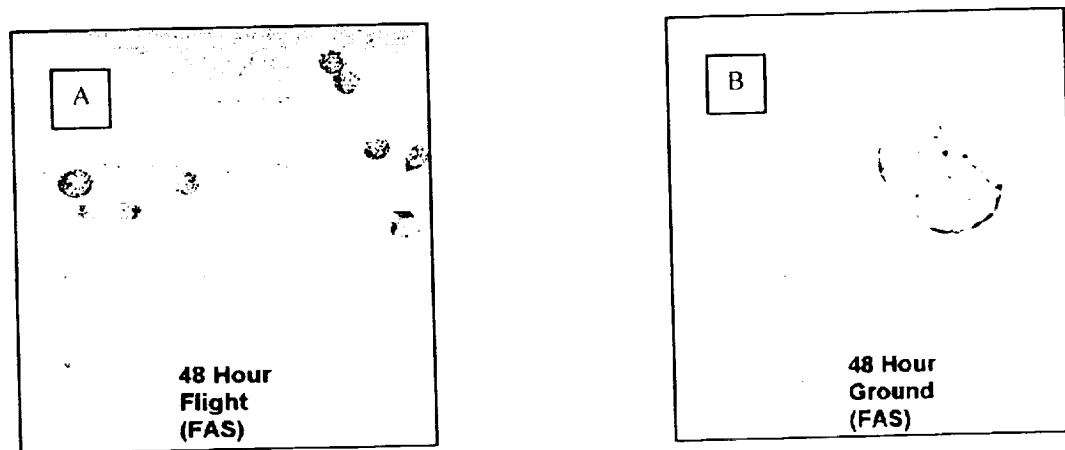


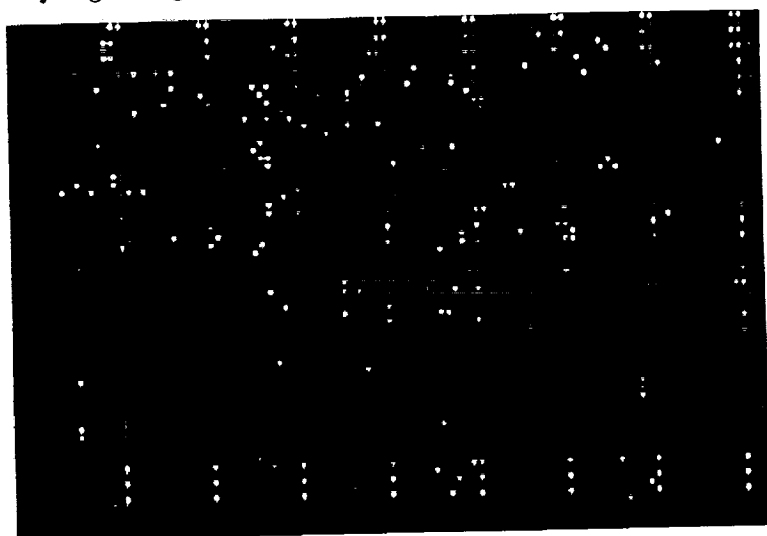
Figure 9. Human lymphoblastoid cells reacted with an antibody to a specific membrane-associated cell death factor (FAS), shown as red dots in the flown cells (A). The left panel (B) shows that in the ground control, the red staining cells are significantly less numerous than in the flown sample.

While this cell death-related factor can be induced by chemicals or antibodies on the ground, in space it is produced without these agents. This difference between production of the factor by cells in flight and on the ground has significant potential for commercial application in factor-induced cell aging and cancer treatment.

In addition to the cell surface differences in flown human lymphocytes (Jurkat, a lymphoblastoid cell line), gene expression was evaluated in order to gain information useful to commercial

companies for drug design and gene therapy treatments. The BioDyn Project Manager and collaborators at the University of Texas applied Microarray gene technology (Research Genetics GeneFilters™) to evaluate expression of more than 16,000 known human genes in the human lymphocytes flown on STS-95. The cells, filtered from culture medium in the BPMs at 24 and 48 hours after growth stimulation in microgravity, were lysed with a solution containing guanidinium isothiocyanate followed by freezing at -80° C for the duration of the mission. Total RNA was extracted post-flight and applied to GeneFilters™ impregnated with cDNA for the genes analyzed. An example of results of a microarray GeneFilter™ assay evaluating expression of 4,324 genes is shown in Figure 9 below.

Figure 9. Microarray of gene regulation in space flown human lymphocytes compared to ground controls.



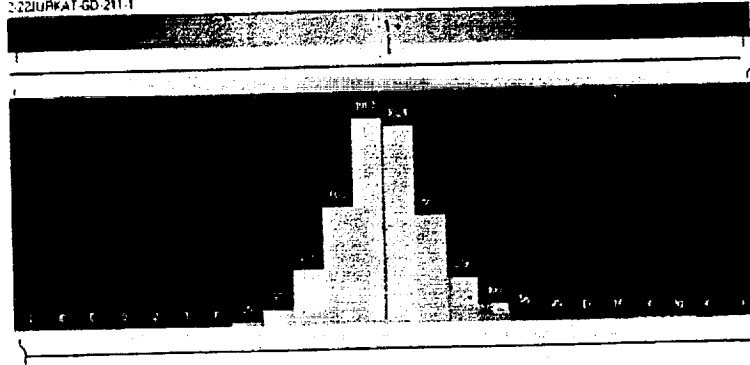
Red = up regulation
Yellow = no change
Green = Down regulation

Magnitude of change will be found on report (following page)

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222JURKAT-GD-211-1

305JURKAT FLT211PH-1



Histogram summarizing changes in all hybridization 3/5/99 Jurkat
between ground and flight GeneFilters™ Dr. Lewis

Each colored dot represents binding of a gene transcript in the RNA extracted from flight or ground control cells with a complimentary sequence of a known gene impregnated into the filter.

Our results showed significant differences between flight and ground controls in expression of genes regulating cell cycle, apoptosis, heat shock response, metabolism, structural proteins, cancer, intracellular signaling, mitochondrial proteins, and a number of transcription factors and DNA binding proteins. Up-regulation of plectin, gelsolin precursor, dynactin, c-nap 1, and tropomodulin genes is of particular interest since all are mediators of cytoskeletal organization. This new knowledge of gene expression during spaceflight provides commercial companies with information that can be used in the development of gene therapies. Additional flights are needed to determine how we may use this information to improve ground-based production of cancer-fighting factors. This is a new area and additional commercial affiliations and support should be actively sought and identified for the future.

2. Anti-Cancer and Anti-Alcoholism Products from Plant Cells: University Of Michigan and Industry Affiliate, Hauser Chemical Co.

Sample analyses of the University of Michigan-Hauser Chemical Company plant cell project were complete in July. Results show that the soybean cells in microgravity are active producers of anti cancer and anti-alcoholism compounds. Thus feasibility for the commercial process of plant cell culture and derivation of drugs in microgravity is now established. Plant cells were

Figure 10.

Products from Plant Cells in Culture



Industry Affiliate:
Hauser Chemical Co.
Consultant: Univ. Michigan

Objective: Evaluate microgravity environment for upregulation of synthesis of medically important metabolites by plant cells.

Genisten and daidzein are isoflavonoids with anti-cancer activity

obtained from leaf cells of soybean plantlets similar to the one shown in Figure 10. The isolated cells were loaded into the BPM syringes pre-flight and placed on a pouch at ambient lighting and temperature during the mission. Twenty-four hours before landing, the pouch was re-stowed in the CRIM. Post-flight, samples were evaluated for genisten and daidzein at the University of Michigan. STS-95 is the third flight of this plant system and results have consistently shown plant secondary metabolites to be a viable commercial space product.

COMMERCIAL SUPPORT FOR STS-95

The amount of commercial support for the STS-95 payload totaled more than \$300,000 (Appendix I, VG #6) in the form of reagents, materials, samples, pre- and post-flight analyses, use of personnel and equipment in the PI laboratories, and travel of the PIs to the Cape to assist with the preparations for their experiments. Hands-on assistance of the industry and university affiliates was critical to the success of these commercial development ventures since BioDyn's laboratory staff consisted of the Project Manager/PI, one tissue culture technician, a post-doctoral fellow, an administrative assistant and several unpaid graduate and undergraduate students. All of the in-kind funding support provided by the industry affiliates amounts to free support to NASA and advances NASA's objectives to develop commercial products in space. The industry and university affiliates are actually paying to fly their commercial experiments on the Shuttle. The information gained and database expansion is provided without cost to NASA (as opposed to the NASA NRA system in which investigators are paid by NASA to fly experiments). The 100% success of the BioDyn Payload on STS-95 is directly in alignment with NASA's commercial space product development goals.

POSTSCRIPT

On February 19, 1999, the acting CMDS Director officially terminated the BioDyn Project effective April 30, 1999. All of the industry affiliates and associated university investigators were notified of this action by Dr. Lewis, and in some cases, by the acting CMDS Director. Dr. Lewis has referred these affiliates to another CSC if they desire to continue development of their products in space.

This abrupt action taken by UAH was surprising in light of the achievement of 100% of the science and hardware objectives on the STS-95 mission flown in October 1998. The BioDyn Project brought over \$300,000, in the form of in-kind support provided by the industry affiliated product areas, to the NASA CSC program. BioDyn's achievement on STS-95 is in direct conformance with NASA's definition of industry commitment and fully supports NASA's commercial space development directives. Product development goals were met for all of BioDyn's product areas and two new automated hardware devices were qualified for use on Space Station. In fact, based on BioDyn's experience on about ten previous missions and successes on STS-80 and especially on STS-95, the NASA system had already moved BioDyn to the top of the queue of projects among the CSCs for STS-107 and we had begun working requirements. Plans for leveraging cash commitments from the industry affiliates for this mission were being drafted.

Termination of the BioDyn Project by August 31, 1999 has not permitted sufficient time to complete the analyses of the STS-95 samples for the protein (aging) product development area. These analyses will continue, though unfunded by the CMDS, until completion expected in May 2000.

Submitted by:



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APPENDIX I

Supporting Viewgraphs

THE BIODYN PAYLOAD ON STS-95



**Commercial
Space Center**

UAH CMDS

**BioDyn
Project Manager
Marian L. Lewis, Ph.D.**



BioDyn's Industry- Driven Target Products

Tissue Engineering

- o Bone implants
- o Heart patches

Protein Products

- o Recombinant proteins to prevent tissue rejection.
- o Cell aging factors

Plant Cell Products

- o Anti-cancer
- o Anti-alcoholism



BioDyn's Industry Affiliates

Tissue Engineering

- o Millenium Biologix, Inc
Univ. of So. Carolina

Protein Products

- o SYNTHECON, INC.
Univ. of Texas

Plant Cell Products

- o Hauser Chemical
Univ. Michigan



Selection Criteria

<u>Criteria</u>	<u>Synthecon Protein/Aging Transplnt/lyms</u>	<u>Millenium Tiss. Eng Bone/heart</u>	<u>Hauser Chem Plant prod. Cancer/Aleo</u>
• Need for Space Demonstrated	Yes	Yes	Yes
• Target Market Exists	>\$200mill	>\$5 bill	>\$300bill
• Space Opportunity	need ~5 flts	need ~5 flts	need ~5 flts
• Commitment. (in kind/flt)	\$125 K/flt	\$135K/flt	\$75 K/flt
• Internatl collab bene US	NA	Artificial Scaffold	NA
• Animal/ACUC	NA	In place	NA

5.



STS-95-BioDyn Product Supporting Flight and Ground Based Hardware

<u>Type</u>	<u>Provided by</u>
BioDyn Bioreactor	SHOT/Synthecon/UAH
BPMs (Bioprocessing Modules)	UAH
ABPM (Automated BPM)	UAH

6.



Affiliate Resource Commitment to BioDyn on STS-95

<u>Affiliate</u>	<u>Product</u>	<u>Commitment</u>
Synthecon Univ. TX	Recombinant proteins Cell aging factors	~\$75K in kind ~\$50K in kind
Millenium Univ. S. C.	Bone implants Heart patches	~\$75K in kind ~\$55K in kind
Hauser Chem. U. Mich.	Plant cells: Anti-cancer Anti-alcoholism compnds.	~\$75K in kind
TOTAL		\$330,000

APPENDIX II

Biodyn Related Publications and Presentations

BioDyn Related Publications and Presentations

Peer Reviewed Publications

Lewis, M.L., Bowman, P., Cubano, L.A., Piepmeier, E.H. Gene expression in space flown human lymphocytes (Jurkat) evaluated by microarray gene analysis. In prep. (1999).

Cubano, L.A., and Lewis, M.L.. Increased levels of Fas in the Medium of Cells Flown on the Space Shuttle on STS-80 and STS-95. In prep for Exp. Cell Res. 1999.

Cubano, L.A. and Lewis, M.L.. Effect of vibrational and spaceflight stress on regulation of heat shock proteins HSP-70 and HSp-27. In prep for J. Cellular Biochem. 1999.

E. H. Piepmeier, J. E. Kalns, K. M. McIntyre, M. L. Lewis. Prolonged Weightlessness Affects Promyelocytic Multidrug Resistance, Experimental Cell Research, 237(2):410-418 (1997).

Hughes-Fulford, Millie and Marian L. Lewis. Effects of Microgravity on osteoblast growth activation. Experimental Cell Research. 224: 103-109, 1996.

Abstracts Published

Hughes-Fulford, K. Nelson, S. Blaug, C.G. Summer, B.D. Lukefahr and M.L. Lewis. MC3T3-E1 osteoblasts grown in microgravity on STS-56 have reduced cell growth, glucose utilization with altered actin cytoskeleton and increased prostaglandin synthesis. ASGSB Bulletin Vol. 7:, (1993).

Neil, G.A., L. A. Love-Homan, C. Summer, D.W. Sammons and M.L. Lewis, Human splenic B cell activation *in vitro* is not impaired by microgravity (ug). ASGSB Bulletin Vol. 7:, (1993).

Gruener, Raphael R. Roberts and R. Reitsstetter. Exposure to microgravity alters properties of cultured muscle cells. ASGSB Bulletin Vol. 7:, (1993).

Principato, M.A., B.D. Lawless and M.L. Lewis. Superantigen-mediated T cell receptor stimulation in zero gravity. ASGSB Bulletin Vol. 7:, (1993).

M.L. Lewis, M.A. Principato, B.D. Lawless, W.C. Kapp, S.L. Strobl and A.C. Ochoa. Effects of microgravity on leukocyte growth control and function. Molecular Biology of the Cell (Abstracts) 4:450a (1993).

Lewis, M.L. and M. Hughes-Fulford. Use of RT-PCR to evaluate microgravity effects on cells. American Society for Gravitational and Space Biology (ASGSB) Bulletin 8:82 Abs. #159 (1994).

Lewis, M.L., Gravity sensing in human lymphocytes (Jurkat) involving the microtubule cytoskeleton. Gravitational and Space Biology Bulletin 10:47 (1996)

Clunie, J.C., M.L. Lewis, D.T. Albright, and J.K. Baird. A search for gravitational effects in diffusion. In: Space Processing of Materials. SPIE-The International Society for Optical Engineering, 2809:244-246 (1996).

Krock, L.P., G.B. Kemper, M.L. Lewis, and M.G. Davis and E.H. Piepmeier. Microgravity influences adriamycin distribution in HL60 and multidrug resistant HL60/ADR cells. Aerospace Medical Assoc. 1996 (abstr.).

Hatton, J.P., D.A. Schmidt, F. Gaubert, Y. Darsel, S Roquefeuil, M.L. Lewis, and J.P. Cazenave. The effect of Microgravity on protein kinase c isoform quantity and localisation in a human leukocytes. Gravitational and Space Biology Bulletin, 11: Abstr # 120 (1997).

Lewis, M.L., J.A. Reynolds, L.A. Cubano, C.A. Yancey. Increase in Fas/APO-1 protein and apoptosis in space flown human T cells (Jurkat). Gravitational and Space Biology Bulletin, 11: Abstr # 140 (1997).

Lewis, M.L., Reynolds, J.A., Cubano, L.A., Yancey, C.A., Lawless, B.D. and Piepmeier, E.H.. The cell death factor, sFas/APO-1, as a regulatory mechanism of apoptosis and population growth response in space flown lymphocytes. Gravitational and Space Biology Bulletin, 12: (1998).

Presentations at Professional Meetings

Lewis, M.L. and J.M. Cassanto. Automated, multiple-sample minilabs provide significant cell biology and space bioprocessing data from Shuttle middeck research. Space Station Meeting, Washington DC, 1992.

Lewis, Marian L.. Materials Dispersion and Biodynamics Project. First Annual Space Station Freedom Utilization Conference Proceedings, August 3-6, 1992.

Cassanto, John R. and Marian L. Lewis. Commercial Materials Dispersion Apparatus on the Space Shuttle. IAF section, World Space Congress, Washington D.C., Aug. 29-Sept. 5, 1992.

Lewis, Marian L. and B. DeSales Lawless. Results of STS-43 Cell tests in the Materials Dispersion Apparatus (MDA). American Society for Gravitational and Space Biology, Tucson, AZ. Poster # 50. October 20-24, 1992.

Hughes-Fulford, K. Nelson, S. Blaug, C.G. Summer, B.D. Lukefahr and M.L. Lewis. MC3T3-E1 osteoblasts grown in microgravity on STS-56 have reduced cell growth, glucose utilization with altered actin cytoskeleton and increased prostaglandin synthesis. ASGSB Annual Meeting (1993).

Neil, G.A., L. A. Love-Homan, C. Summer, D.W. Sammons and M.L. Lewis. Human splenic B cell activation *in vitro* is not impaired by microgravity (ug). ASGSB Annual Meeting (1993).

Gruener, Raphael R. Roberts and R. Reitstetter. Exposure to microgravity alters properties of cultured muscel cells. ASGSB Annual Meeting (1993).

Principato, M.A., B.D. Lawless and M.L. Lewis. Superantigen-mediated T cell receptor stimulation in zero gravity. ASGSB Annual Meeting (1993).

M.L. Lewis, M.A. Principato, B.D. Lawless, W.C. Kapp, S.L. Strobl and A.C. Ochoa. Effects of microgravity on leukocyte growth control and function. American Soc. for Cell Biology Annual Meeting (1993).

Lewis, M.L. and M. Hughes-Fulford. Use of RT-PCR to evaluate microgravity effects on cells. American Society for Gravitational and Space Biology ASGSB Annual Meeting (1994).

Lewis, M.L., Gravity sensing in human lymphocytes (Jurkat) involving the microtubule cytoskeleton. ASGSB Annual meeting 1996.

Clunie, J.C., M.L. Lewis, D.T. Albright, and J.K. Baird. A search for gravitational effects in diffusion. In: Space Processing of Materials. SPIE-The International Society for Optical Engineering Meeting 1996.

Krock, L.P., G.B. Kemper, M.L. Lewis, and M.G. Davis and E.H. Piepmeier. Microgravity influences adriamycin distribution in HL60 and multidrug resistant HL60/ADR cells. Aerospace Medical Assoc. 1996.

Hatton, J.P., D.A. Schmidt, F. Gaubert, Y. Darsel, S Roquefeuil, M.L. Lewis, and J.P. Cazenave. The effect of Microgravity on protein kinase c isoform quantity and localisation in a human leukocytes. ASGSB Annual Meeting 1997.

Lewis, M.L., J.A. Reynolds, L.A. Cubano, C.A. Yancey. Increase in Fas/APO-1 protein and apoptosis in space flown human T cells (Jurkat). ASGSB Annual Meeting 1997.

Lewis, Marian L. Potential of microgravity for tissue engineering. Abastracts: Recent Advances in Fermentation Technology (RAFT II) Conference, November 15-18, 1997. San Diego, CA. Sponsored by the Society for Industrial Microbiology (SIM) and the Biochemical Technology (BIOT) Division of the American Chemical Society (ACS)

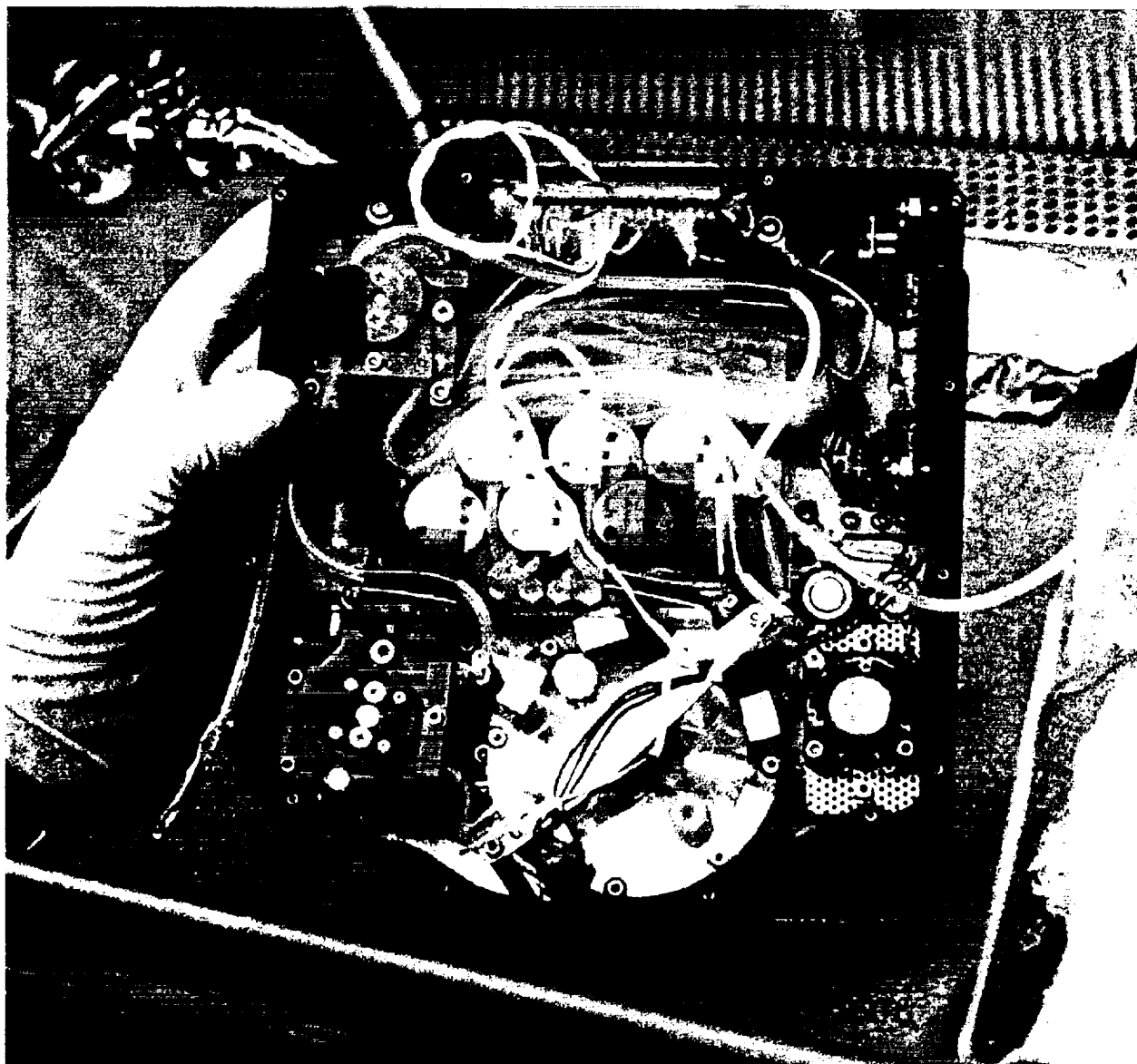
Lewis, M.L., Reynolds, J.A., Cubano, L.A., Yancey, C.A., Lawless, B.D. and Piepmeier, E.H.. The cell death factor, sFas/APO-1, as a regulatory mechanism of apoptosis and population growth response in space flown lymphocytes. ASGSB Annual meeting 1998.

APPENDIX III

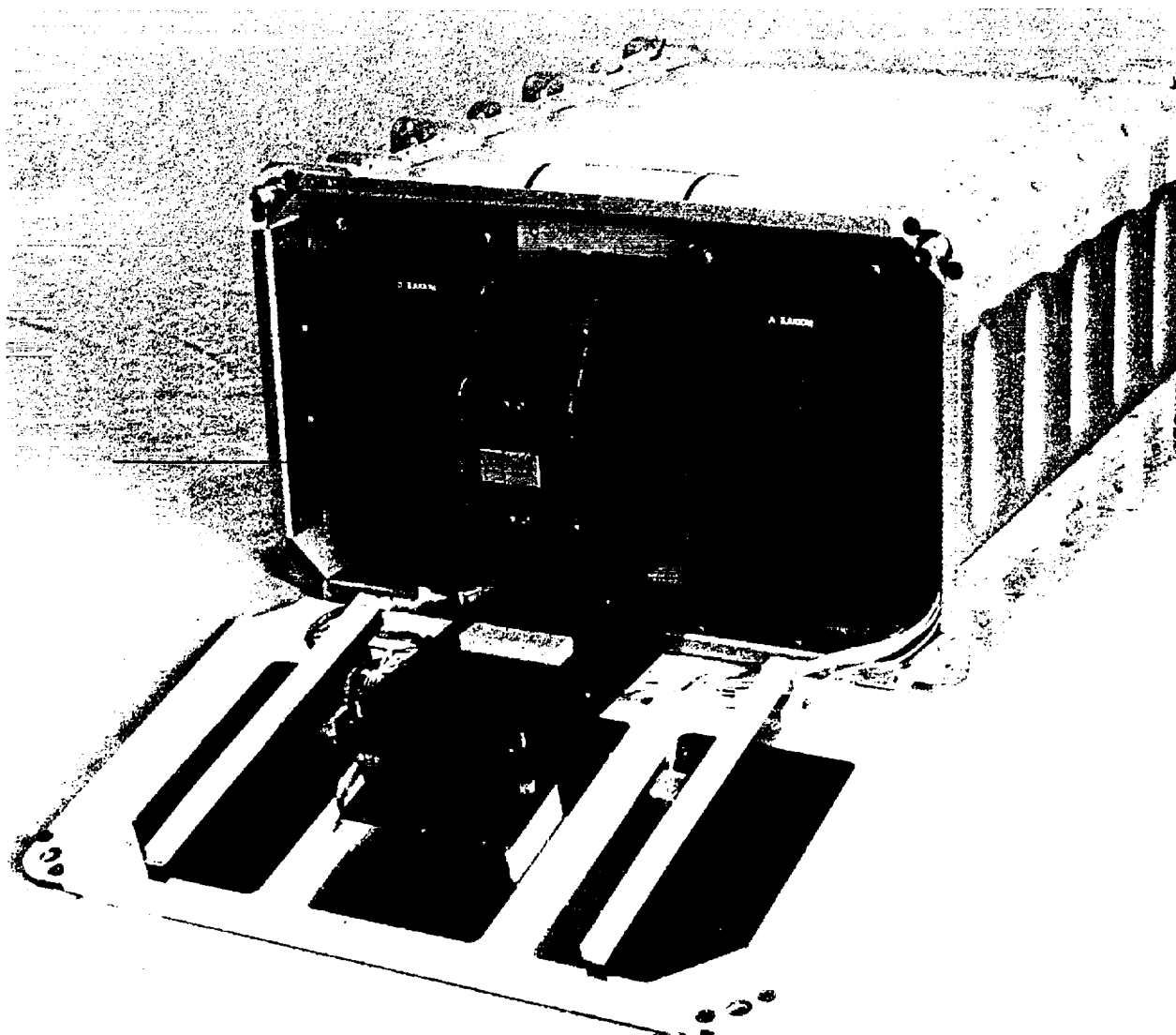
STS-95

**BioDyn Bioreactor (BB) and
ADSEP Processing Facility**

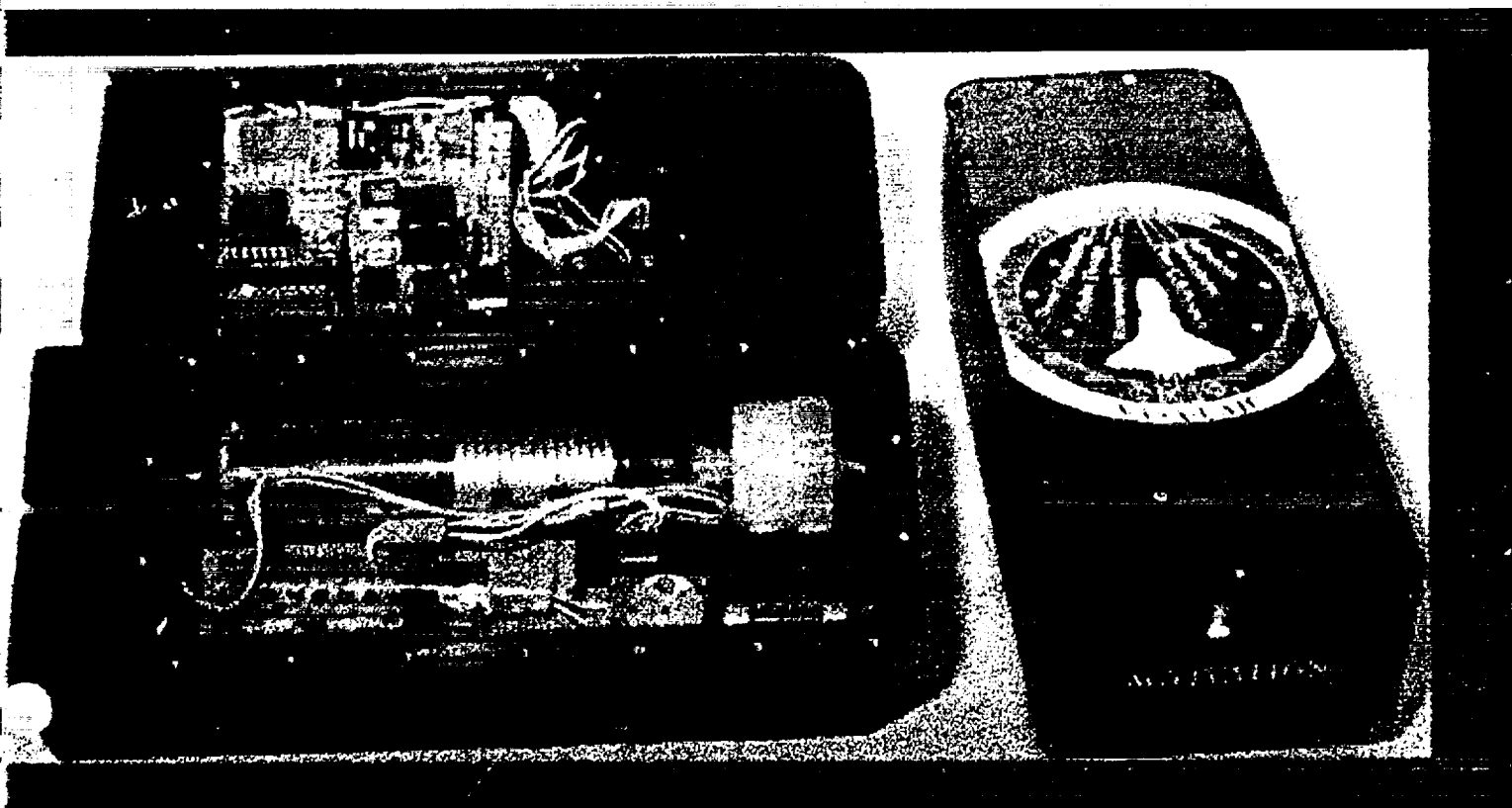
**and an
Automated Bioprocessing Module (ABPM)**



BioDyn Bioreactor internal components packaged in an ADSEP Cassette.



ADSEP Processing Facility locker showing the STS-95 BioDyn Cassette (arrow) in the middle section of the unit.



Automated Bioprocessing Module (ABPM). A complete unit (right) is a brick sized aluminum box. With top plate removed, the lower view shows the culture chamber with three syringes, a 30 ml and two 5 ml sizes. (The top view is the underside of the culture chamber showing the electronics for automation). A filter unit in line of the 30 ml syringe allows filtration of cells from medium prior to the addition of fixative to the cells. A motor in the barrel of the 30 ml syringe drives the plunger to accomplish fluids exchanges. At approximately 4 hours after reaching orbit, John Glenn pressed the switch marked "Activation" to initiate the experiment. All other manipulations were automatic including cell activation and fixation. The ABPM operated within the CRIM.

METRO/STATE

PAGE 22A

UAH researchers to train Glenn on shuttle experiment

By Kent Faulk
News staff writer

HUNTSVILLE — Marian Lewis remembers when U.S. Sen. John Glenn made his first space flight aboard a Mercury capsule on Feb. 20, 1962, becoming the first American to orbit the Earth.

"I never thought in my wildest dreams that I would ever have an opportunity to work with him on a space flight mission," said Ms. Lewis, a research biologist at the University of Alabama in Huntsville.

Next week, Ms. Lewis and two other UAH researchers will hold the first of several training sessions at the Johnson Space Center in Houston with Glenn and space shuttle mission specialist Scott Parazynski to show the two men how to operate a UAH experiment package.

Glenn, 76, of Ohio, is making his return to space aboard the space shuttle *Discovery* on Oct. 29 to do research on the effects of weightlessness on aging. Among the experiments he will work with during his

"Normally before any of our space flight payloads fly we make the crew familiar with the science, the hardware and the operations involved."

Marian Lewis
UAH biologist

nine days in space is the UAH experiment package called the Biodynamics and Space Cell Culture (Biodyn) experiment pack.

Biodyn, managed by UAH's Consortium for Materials Development in Space, is designed to foster the commercial development of space through the production, by living cells in the low gravity of space, economically important bio-materials.

The experiments have been designed to address medical conditions including those related to aging, such as heart and vascular disease, bone degeneration, diabetes and cancer.

Biodyn will carry experiments for

UAH-affiliated companies involved in tissue engineering to create bone implants and heart muscle patches. It also includes growing plant cells capable of producing anti-cancer and anti-alcoholism compounds.

Another experiment will grow cells to produce a genetically engineered protein that should help prevent the rejection of organ and tissue transplants.

"We are very excited about it," Ms. Lewis said. "We'll have an opportunity to work with a legend."

Ms. Lewis, mission manager Niki Myers and Francis Wessling, associate director of the consortium, will train Glenn and Parazynski.

"Normally before any of our space flight payloads fly we make the crew familiar with the science, the hardware and the operations involved with our payload," said Ms. Lewis, who has had cell-growth experiments aboard 15 shuttle flights.

Ms. Lewis said they will be with Glenn and Parazynski two to three hours on Tuesday for a crew-familiarization briefing.

After a briefing on the science and hardware, Glenn will get a couple of hours of hands-on training with the biodyn experiment package, she said.

UAH researchers will go back

later to work with Glenn and Parazynski on the experiments, Ms. Lewis said.

Glenn won't be the first U.S. senator to work with a UAH experiment in space, said Chuck Lundquist, di-

rector of the consortium.

Sen. Jake Garn of Utah, who became the first — and so far only — senator to fly into space in 1985 aboard *Discovery*, worked with a UAH experiment, Lundquist said.

Exponent

September 24, 1998

Vol. 30, Issue 4

Glenn
Continued from page 1

at all," Ms. Myers said. "You notice two things about him right away; the sparkle in his eyes and his energy. He is not deterred by age. Sen. Glenn is very agile and has eagerly completed all his training exercises. To say he has a child-like excitement about the mission is an understatement."

Ms. Myers, a Franklin, Tenn., native who recently graduated with a bachelor's degree in biology, describes her position as research associate with the university's Consortium for Materials Development in Space (CMDS) program as "living her dream."

As mission manager for the experiment package, Myers has responsibility for managing the details of the shuttle flight payload.

"Niki has that rare ability to focus her considerable enthusiasm to work with efficiency and with determinations," said Marian L. Lewis,

Senior Research Associate at UAH and project manager of BioDyn.

"Niki's calm, professional, tactful, and efficient attitude inspires confidence in all of us who work with her, even John Glenn and Scott Parazynski, the prime astronauts operating the BioDyn Payload. All of us know we can always depend on her good judgment and best effort," Lewis added.

As a youngster, Myers toured UAH labs and research facilities as often as she could as part of Space Camp training at the US Space & Rocket Center in Huntsville. "It made things much more real for me to actually see what was going on; nothing beats the hands-on approach to learning," she said.

Myers will return to UAH next spring to pursue a masters' degree in biology. Her advice to those who dream to focus her considerable enthusiasm to work with efficiency and with determinations," said Marian L. Lewis,

UAH grad trains with Glenn

Joyce Anderson-Maples
University Relations

For Niki Myers, enthusiasm is a contagious thing. There's not a doubt in her mind it clinched her role as mission manager for an experiment package for next month's shuttle Discovery flight and she's confident it will help her become an astronaut in the future.

Meanwhile, that enthusiasm has helped Ms. Myers earn what she describes as a "dream come true," conducting training sessions with John Glenn, a four-term US Senator and the first American to orbit the earth.

Sen. Glenn will be a payload specialist aboard STS-95, which is scheduled to be launched on Oct. 29. On that flight, Glenn will help conduct a number of life science experiments being managed by UAH. The experiment package is called the



STAR GAZING—UAH Graduate Niki Myers hangs out with astronaut Sen. John Glenn. Myers is mission manager for an experiment package for next month's shuttle Discovery flight. — Photo courtesy University Relations.

Biodynamics and Space Cell clipping I could get my hands on about space travel including those on Glenn, Alan Shepard, Neil Armstrong and other early astronauts who contributed to America's space program.

"Since I was a little girl I

"Before meeting Sen. Glenn, I envisioned him to be this real dignified older gentleman... a little hard to relate to; but that wasn't true

Glenn
Continued on page 3

Glenn to conduct UAH experiments on shuttle flight

When Sen. John H. Glenn

Jr. makes his second journey into space next month, some UAH experiments while aboard STS-95. The UAH will be spent conducting life science experiments managed by UAH.

The 77-year-old Glenn was the first American to orbit the earth 36 years ago. He returns to space aboard the shuttle Discovery for NASA's TS-95 mission. The launch is scheduled Oct. 29, 1990.

Research scientists from UAH have spent hours with Glenn, conducting training sessions with Glenn on the experiments. These UAH scientists include project manager Marian L. Lewis and mission manager Niki

bone implants and heart muscle patches. The experiment package includes plant cells capable of producing anti-cancer and anti-alcoholism compounds in a microgravity environment.

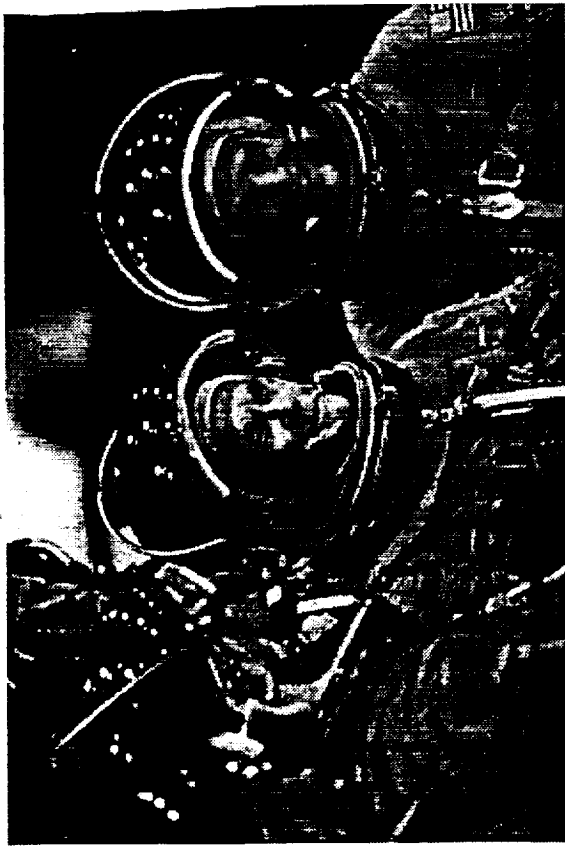
Hardware aboard the shuttle, developed by UAH and its affiliates Syntheon Inc. and Space Hardware Optimization Technology Inc., will also grow cells that produce a genetically engineered protein that should help prevent rejection of organ and tissue transplants.

"All of these biomedical products have great humanitarian value and together occupy an existing commercial market niche estimated in value in the billions of dollars," according to project manager UAH Research Scientist Marian L. Lewis. "The results could benefit millions of Americans and other people worldwide."

For example, simple heart muscle patches can be developed on Earth, but multi-layered patches that could replace damaged heart muscle must be produced in a gravity-free environment, according to Lewis.

Those multi-layered patches could eventually reduce the need for heart transplants, Lewis said. There are more than 50,000 people each year needing a heart transplant to survive and there are only 2,000 donors available annually.

Another experiment involves UAH industry affiliate Millennium Biologix



THE RIGHT STUFF—John Glenn, the 77-year-old astronaut, and some of his crew mates at the Johnson Space Center in Houston. —Photo by Robert A. Reeder of *The Washington Post*

Glenn returns to space

Glenn's first trip into space took place on

February 20, 1962, aboard a Mercury capsule, Friendship 7. He orbited the planet three times and spent almost five hours in space.

The 77-year-old, four-term U.S. Senator from Ohio, will now return to space aboard the shuttle—

some 36 years after his initial flight into outer space. The STS-95 mission is expected to last eight days and 21 hours.

Glenn is traveling as a payload specialist on the upcoming mission. He will take part in numerous experiments to study the connection between weightlessness and the

Inc. The company will prepare human bone transplants by seeding the company's artificial material with human bone cells.

This tissue forms more readily in microgravity and could lead to revolutionary products from synthetic bone. These products have potential for dental implants, long bone grafts and coating for orthopedic im-

those microcapsules could be more uniform in a microgravity environment and thus improve the product's effectiveness.

The Biodyn payload is managed by UAH's Consortium for Materials Development in Space and is sponsored by the Space Processing Division of NASA's Office of Space Access and Technology.

Revered astronaut to carry experiments from UAH in space

By MIKE SALINERO
Times Staff Writer

When 76-year-old John Glenn takes off for space later this year, he'll be carrying along experiments from the University of Alabama in Huntsville.

Glenn — one of the most famous U.S. astronauts and a former U.S. senator from Ohio — will conduct experiments that could decrease the need for heart transplants, improve bone implants and end diabetics' reliance on needles for insulin.

The UAH package of experiments is called Biodynamics and Space Cell Culture, or the "biodyne" payload for short.

The STS-95 mission is expected to take off Oct. 29 and last eight days and 21 hours. Glenn will also take part in numerous experiments to study the connection between weightlessness and the aging process.

Glenn will have prime operation of the biodyne payload on the shuttle Discovery's STS-95 mission. He will be assisted on the UAH experiments by mission specialist Scott Parazynski.

Project manager Marian L. Lewis will head a team of UAH scientists that will leave for Houston on Monday and will meet with Glenn Tuesday. Lewis will be accompanied by mission manager Niki Myers and Francis Wessling, associate director of the Consortium for Materials Development in Space.

Lewis said that based on previous shuttle experiments in tissue engineering, some transplantable materials can be developed better in microgravity. One material would be a piece of heart muscle that can be produced outside the body.

Lewis said this "heart patch" is not being implanted now, but if it can be perfected, it could lessen the need for heart transplants dramatically. Each year there are approximately 50,000 people needing heart transplants to survive, but only about 2,000 donors.

"So one of the experiments John Glenn will be duplicating in space is one to determine the fea-



The Associated Press

Sen. John Glenn, D-Ohio, prepares to board a space shuttle mockup for a training simulation at the Johnson Space Flight Center in Houston on Thursday. Glenn is scheduled to return to space in October and will carry experiments from UAH.

sibility of making heart patches," Lewis said.

UAH is working with a company called Millennium Biologix Inc. on bone implants. The company has developed a "scaffold" on which it hopes bone cells will grow. If the scaffolding works, it can be used in treatments for osteoporosis, for dental implants along the jaw and for better-functioning hip replacements.

Lewis said previous experiments indicate the bone cells associate better to form tissue in microgravity.

"The cells have freedom in microgravity to form cell-to-cell interactions, where on the ground if you have a number of cells in a culture, by gravity they settle to the surface and they can't move very well to associate," she said.

UAH is working with VivoRx Inc. on an experiment to develop an encapsulating material for cells that secrete insulin, a hormone that helps the body metabolize sugar.

Huntsville Times

Friday, June 26, 1998

Diabetics now must take insulin injections daily because their bodies don't produce enough. The implant VivoRx is working on would last for months and free diabetics from the daily injections.

The encapsulating material, implanted in the skin, would secrete insulin in uniform amounts.

At the same time, the material would protect the cells that produce the insulin from the diabetic's own immune system.

"Our objective is to try to form a more uniform molecular sieve for allowing the cells to be inside the capsule and secrete insulin to the outside," Lewis said. "Microgravity provides an environment that allows formation of more-uniform capsule material for the cells."

The encapsulating material is made of a derivative of seaweed. The material forms a lattice that protects the cells from destruction from the immune system while secreting the insulin.

"Microgravity apparently — based on previous experiments — produces a superior molecular assembly ... a more uniform lattice," Lewis said.

Another experiment Glenn will be working on is a genetically engineered protein produced in a culture. Synthecon Inc. of Houston, which is developing the protein, hopes it can be marketed to prevent rejection of transplanted material.

Glenn first went to space Feb. 20, 1962, aboard a Mercury capsule, Friendship 7. He spent five hours in space, becoming the first man to orbit the earth. He circled the globe three times.

APPENDIX C

Sintered and Alloys Metals Interim Report

DIFFUSIONAL MODELING OF GRAIN GROWTH OF LIQUID PHASE SINTERED CO-CU SAMPLES IN MICROGRAVITY

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ABSTRACT

This paper discusses the diffusion controlled grain growth of Co-Cu samples processed under microgravity. Twelve powder compact samples with solid volume fraction ranging from 50% to 70% were processed at 1473 K during liquid phase sintering (LPS) experiments aboard sounding rockets and Space Shuttle missions. Processing time ranged from 2.5 to 66 minutes.

The effects of liquid volume fraction and processing time on grain growth for short times sintering are discussed. Experimental results of grain size measurements and grain-coarsening rate are presented. The diffusional layers in Co grains were captured by Scanning Electron Microscope (SEM) in 70vol%Co-Cu sample with processing time 17 minutes. The diffusion controlled solution reprecipitation and Cu penetration into Co grains result in two different layers around Co grains. A shrinking core model is developed and used to investigate the mechanisms and the kinetics of those diffusion layers.

INTRODUCTION

The Co-Cu system has been studied in some detail because the density of cobalt and copper are similar so that gravitational effects in LPS are minimized. However, even with a small (about $0.5\text{-}0.8\text{g/cm}^3$) density difference between two phases [4], it is not possible to eliminate buoyancy effects such as pore migration and differential settling in unit gravity. These are processes that can not be eliminated by density matching alone. These effects are still present in microgravity processed samples and are functions of particle agglomeration and coalescence driven by surface tension, capillary forces and other interaction forces. Processing in microgravity environment provides a unique opportunity to isolate transport from sedimentation mechanisms, thereby permitting the study of transport effects on macrostructure, pore morphology and microstructure.

The modeling to predict particle coarsening is technologically important because of the dependence of properties on microstructure [5]. In 1961, Lifshitz et al. stated (the low volume fraction theory) that the cube of the average particle radius grows proportional with annealing time if mass transport is by diffusion [6]. They also showed particle size distributions in the limiting case of long annealing times. During the last decade numerous experiments have been conducted and theoretical approaches have been attempted to improve the LSW theory with the focus on prolonged sintered particles. The particle growth in rearrangement stage and solution-reprecipitation stage has been ignored as it is difficult to capture in unit gravity studies. In this paper, the recent experimental results from microgravity processed Co-Cu samples

will be presented and some qualitative analysis on diffusion controlled grain growth in short sintering time will be discussed.

II. EXPERIMENTAL DETAILS

LPS of twelve Co-Cu powder compacts were conducted aboard four Consort sounding rocket flights and three Space Shuttle missions. The compositions were selected to yield 30, 40 and 50 volume percent of the liquid copper phase during sintering. The furnace module for these flights was configured to exceed the melting point (1356 K) of copper. Three Co-Cu samples of different composition were processed at 1373 K for 2.5 minutes aboard the Consort 4 suborbital sounding rocket, 5 minutes aboard STS-57, 17 minutes aboard STS-60 and 66 minutes aboard STS-63, using the Equipment for Liquid Phase Sintering Experiments (ECLIPSE) flight furnace and quench system which was described elsewhere [7].

Co-Cu green compacts were fabricated from high purity Co and Cu powders. The powders were supplied and graded by Alfa and were used as received without further modification. The Co and Cu powders were weighed in air and blended in a rotary mixer.

The mixed powders were transferred to a die lubricated with zinc stearate. A Carver hydraulic laboratory press was used to exert a compaction pressure of 110 MPa. This pressure was applied for one hour to obtain a green compact with 70% theoretical density, without the use of internal waxes commonly used to prepare LPS compacts. The compaction pressure of 110 MPa and pressing time was selected to minimize forced shape accommodation, compact swelling, and solid skeletal formation within the compact. The cylindrical compacts were of 10 mm height and 18.8 mm in diameter.

The pressed compacts were reduced in a tubular reactor under a flowing gas mixture of 5% H₂ with the balance He, following a time and temperature profile designed to remove contaminating oxides and lubricants. The samples were then separated by stainless steel shims, stacked in a cylindrical stainless steel ampoule and loaded into the flight furnace. For ground processing, the sample diameter was reduced to 12mm and the samples loaded into alumina crucibles prior to insertion into the stainless steel ampoule.

III. RESULTS AND DISCUSSION

The studies on grain growth in sintering process are important because of the practical benefits of improving material properties. Lifshitz and Wagner (low volume fraction theory) studied the grain growth and concluded that the cube of the average particle radius grows proportional to the annealing time if mass transport is by diffusion. The major driving force for grain growth is the decrease in the interfacial energy. Smaller grains have larger chemical potential and are more soluble in the liquid phase. Therefore, smaller grains tend to dissolve and solidify on the surface of larger grains, enhancing grain growth, a process termed Ostwald ripening. As a result, solute will diffuse from small to large particles through the solvent matrix.

So far most ground experiments were limited to low solid volume fraction and focused on Ostwald ripening process. The samples discussed here have high solid volume fractions (from 50vol%Co to 70vol%Co) and were successfully processed in orbit. The effect of composition and processing time on the grain size of those samples is presented in Figure 1. In this figure, the cube of the grain sizes for the three

liquid volume fractions is plotted against the processing time. The linear grain growth rate shows a diffusion controlled grain growth. The rate of grain growth increases with decreasing volume fraction of the liquid phase. This was consistent with previous LPS studies of prolonged sintered samples that showed an increase in the rate of grain growth with increasing grain contact. An examination of Figure 1 shows that the grain growth rate increases as the liquid volume fraction was decreased. This indicated that a smaller separation distance between the grains enhances the mass flux between particles and thus increases the ripening rate.

Given the extent of agglomeration, grain growth appears to be driven by diffusion and grain coalescence. However, detailed microstructure analysis shows that three types of diffusion mechanism coexist for short time sintering. One is liquid diffusion due the concentration gradient, one is the diffusion of liquid Cu into Solid Co particles and the other is solid particles dissolved in liquid Cu matrix. Figure 2 shows a picture of Co grains taken by SEM. Two diffusion layers exist which were never captured before in prolonged sintered samples. Figure 3 shows an enlarged picture for one Co grain. The two different layers shown by different gray scale are separated by dark color grain boundaries. X-ray diffraction tests showed Cu compositions are different between two layers and are different from the inner core and outer liquid phase. Outer layer has higher Cu concentration than that in inner layer. The picture provide direct evidence that concentration gradient exist in liquid phase sintering even though it is hard to determine the exact values using current methods. One possible explanation for the double layer is that the outer layer is formed by solution reprecipitation and inner is formed directly from Cu solid diffusion. Since the dissolution process is much faster than solid

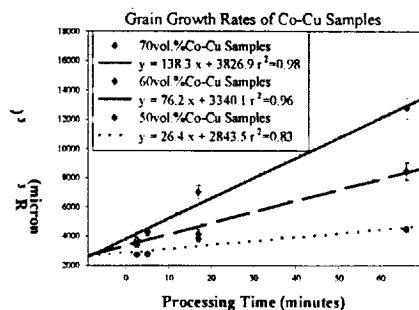


Figure 1 Diffusion Layers in A Co Grain (70vol%Co-Cu Sample, Processing Time 17 Minutes.).

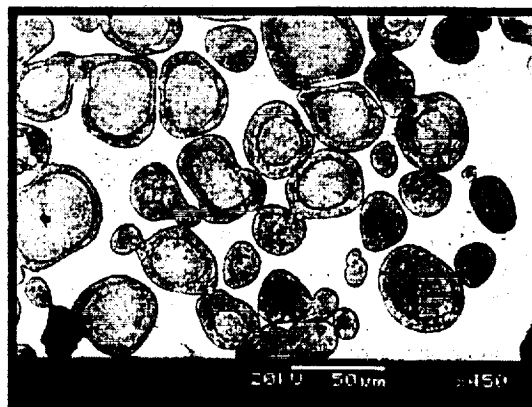


Figure 2 Co Grains showed Diffusion Layers after 17 Minutes Processing (70vol%Co-Cu Sample).



Figure 3 Diffusion Layers in A Co Grain (70vol%Co-Cu Sample, Processing Time 17 Minutes).

state diffusion, the dissolution process can be ignored based on the time scale. The double layer can be verified by a shrinking core model.

Assuming a spherical cobalt particle with radius R dispersed in liquid copper, the concentration profile of copper inside cobalt particles is affected by the diffusion coefficient, concentration gradient and boundary moving velocity v . The governing equation can be translated as following:

$$\frac{Df^2u}{f\xi^2} = (r_0 + vt)^2 \frac{fu}{ft} - (r_0 + vt)v\xi \frac{fu}{f\xi} \quad (1)$$

with $u=(r_0+vt)C_0$ at $\xi=1$ and $u=0$ at $t=0$, u is bounded at $\xi=0$.

This equation can be solved numerically. To make this problem simple, we ignored the concentration changes due to the boundary moving and the diffusion flux can be simplified in following equation [8,9]:

$$\frac{fu}{ft} = \frac{Df^2u}{fx^2} \quad \text{with } 0 \leq x \leq R \quad (2)$$

The analytical solution for this equation is given as following, The copper concentration (C_1) anywhere inside cobalt particle at time t can be calculated as:

$$\frac{C_1}{C_0} = 1 + \frac{2}{\pi\xi} \sum_{n=0}^{\infty} \frac{(-1)^n}{n} \exp[-n^2\pi^2T\xi] \sin[n\pi\xi] \quad (3)$$

where C_0 is the Cu concentration at boundary, ξ is the dimensionless parameter, $\xi = r/R$, T is the dimensionless time, $T=Dt/R^2$. The impurity diffusion coefficient of cobalt in liquid copper is $4.0968 \times 10^{-9} \text{ m}^2/\text{s}$ [10]. The diffusion coefficient for copper in cobalt was approximated as $1.905 \times 10^{-14} \text{ m}^2/\text{s}$. With these diffusion coefficients, it takes less than one second for cobalt to saturate the liquid copper by dissolution. If we set the copper concentration at outer boundary of inner layer as unit concentration, a concentration profile can be plotted in Figure 4. Based on the Thickness of the inner layer, the concentration at inner boundary is about 70% of unit concentration. With the same diffusion coefficients, it takes 50 minutes for copper to reach 70% of the ultimate concentration for solid-solution formation at the center of the cobalt particle at a diameter of 20 micron, which is the case for 66 minutes sintering. The penetration of Cu in the solid to 70% driven by the solid solution could be less than 1 micron if sintering time is less than five minutes. This suggests that, during liquid phase sintering, right after the liquid forms the liquid copper became saturated with cobalt. Then liquid copper started to slowly penetrate into the cobalt particles. For very short time sintering (less than 5 minutes), no layers was observed since they should be thin. In addition, for samples after 66 minutes sintering, only homogeneous layer was observed. Therefore the saturation to form the solid solution was completed. These findings support our mechanism.

The inner layer is similar to what has been described in Fe-Al sintering process [11]. But unlike solid-state interdiffusion, this layer will disappear and form a uniform Co-Cu alloy after long time sintering. Figure 4 shows a concentration profile for the inner layer after 17 minutes diffusion based on the equation 3. The thickness from 70% to 100% is the same as the thickness shown in Figure 3. As the time

increases, the Co core (from 70% to 0%) shrinks. After 66 minutes processing, the α phase solid solution Co core disappears.

The outer layer, on the other hand, is formed by Ostwald ripening, because small particles are easier to dissolve in liquid copper and reprecipitate on larger grains. Around particles, the diffusion fields overlap and are formed due to the local curvature on particles. It can be seen in Figure 3 that the outer layer thickness is not uniform. Places where two particles are close to each other have thinner layers and the areas where particle exposed to liquid Cu have thicker layer. This suggests that the surface energy reduction is restricted by the geometry and the concentration gradient of Co in liquid Cu exists in order to maintain this uneven grain growth. The thickness of inner layer, however, is almost the same, which means the Cu composition at outer boundary of the inner layer is the same anywhere on the boundary. The composition of Cu in the inner layer is only a function of time, not the geometry. This also suggests that the outer is formed by solution-reprecipitation, because the Cu composition is a constant at where the new precipitated layer is formed.

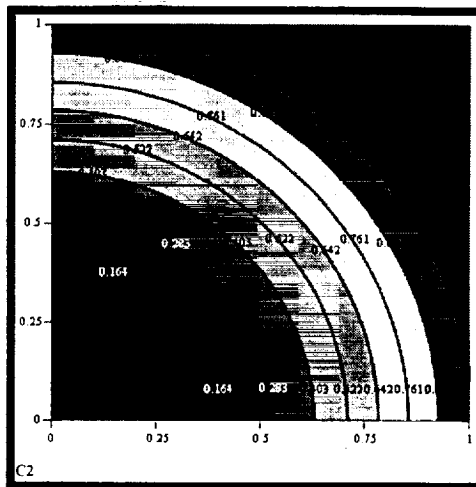


Figure 4. Concentration Profile for Inner Layer Generated Based on Equation 3 after 17 Minutes Diffusion. .

CONCLUSION

Cobalt Grain growth during LPS in microgravity shows a diffusion controlled mechanism. The cube of grain size is proportional to the sintering time. The solid volume fraction and sintering time affect the grain grow rate and the particle size, that differs from some ground sintering results [12]. The diffusion layer was observed during the analysis for the first time, which provide direct evidence for the diffusion controlled grain growth. The shrinking core model can be used to modeling the diffusion processing during short time sintering and more studies needs to be done in order to fully understand this phenomena.

ACKNOWLEDGMENT

This work was supported by NASA and the Consortium for Materials Development in Space at the University of Alabama in Huntsville under contract NAGW-812. WYLE Laboratories and Nextek Inc. are also graciously acknowledged for their involvement. Numerous individuals from both academia and corporate industrial partners have contributed their knowledge, cooperation and support to this project for which the ECLIPSE team is indeed very grateful.

REFERENCES:

1. German, R. M., Liquid Phase Sintering (New York), Plenum Press, 1985.
2. Goetzel, C. G., Treatise on Powder Metallurgy. New York, NY, Interscience Publishers, 1949
3. Kipphut, C. M., Bose, A., Farooq, S., German, R. M.. "*Gravity and Configurational Energy Induced Microstructural Changes in Liquid Phase Sintering.*" Metallurgical Transactions A. 19A, 1988. pp.1905-1913.
4. D. R., Lide, Editor-in-Chief, CRC Handbook of Chemistry and Physics, 72nd Edition, CRC Press, Boca Raton, Ann Arbor, Boston, 1991-1992.
5. S. P. Marsh and M. F. Glicksman, "Global Constraints in Phase Coarsening", Modeling of Coarsening and Grain Growth, TMS Publication, pp. 1-14, 1992.
6. Lifshitz, I. And Slyozov, V., J.Phys. Chem. Solids, 19, 35, 1961.
7. E. Atchley, T. Hamilton, A. Hedayat, J. G. Vandegrift, and J. E. Smith Jr., "*Overview and Preliminary Modeling and Ground-Based Results for the ECLIPSE*", 8th International Symposium on Experimental Methods for Microgravity Materials Science, TMS publication, pp. 87-94(Available in CD-ROM format only), edited by Dr. Robert A. Schiffman. 1996.
8. J. Crank, The Mathematics of Diffusion, Oxford University Press, 1975.
9. H. S. Carslaw, and J. C. Jaeger, Conduction of Heat in Solids, Oxford University Press, 1959.
10. D. B. Butrymowicz, J. R. Manning, and M. E. Read, Diffusion Rate Data and Mass Transport Phenomena for Copper Systems, International Copper Research Association, Inc. 1977.
11. L. Albano-Muller, F. Thummler and G. Zapf, "High-Strength Sintered Iron-Base Alloys by Using Transition Metal Carbides", Powder Met., 1973, vol. 16, pp. 236-256.
12. W. Bender, and L. Ratke, "*Ostwald Ripening of Liquid Phase Sintered Cu-Co Dispersions at High Volume Fractions*", Acta Mater. Vol.46,No.4 pp 1125-1133, 1998.

MODELING OF PORE METAMORPHOSIS IN LIQUID PHASE SINTERED SAMPLES IN MICROGRAVITY

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ABSTRACT

Liquid phase sintering experiments have been conducted on several sounding rocket flights, Space Shuttle missions and on the Mir station. Pore metamorphosis, such as pore breakup and pore coarsening, has been observed in all samples processed on orbit. It has been found that pore behaviors are directly related to the liquid volume fraction of the sample. This paper attempts to show that a critical liquid volume fraction exists where pores bifurcate. The bifurcation produces either smaller pore by a breakup mechanism that is discussed or coalesced pore of very large size. Evidence collected in microgravity shows the presence of this bifurcation. An initiation mechanism is proposed and the results from theoretical analysis and CFD numerical simulation are presented.

I. Introduction

Liquid Phase Sintering (LPS) is a widely used industrial powder metallurgy process. In unit gravity processing, density differences cause sedimentation within the sample, which contributes to solid migration, non-uniform coarsening and anisotropy in the mechanical and material properties of the sintered compacts [1]. Even for systems like Co-Cu with a small density difference between two phases [2], it is not possible to eliminate buoyancy effects such as pore migration and sample slumping in unit gravity. Processing in microgravity environment provides a unique opportunity to isolate transport from sedimentation mechanisms, thereby permitting the study of transport effects on macrostructure, pore morphology and microstructure.

Pores, for example, are not buoyant in microgravity as they are in unit gravity and therefore remain in equilibrium with the solid and liquid phases during LPS. However, in microgravity, removing sedimentation driven convection does not produce a static system. Pore metamorphosis driven by surface tension and capillary forces are still present in microgravity processed samples. Here the terminology of pore is subclassified as a void when low vapor pressure exists and a bubble when inside pressure is high [3]. The surface properties of a pore as well as the shape of the pore are also affected by the size of surrounding particles and the liquid flowing around the pore.

In the past, many powder compact samples from the Fe-Cu, Co-Cu, W-Cu and W-Ni-Cu systems were processed during liquid phase sintering experiments on four sub-orbital sounding rockets, on five different Space Shuttle missions and twice on Mir station. Pore deformation was observed in all samples. Detailed studies have shown that three pore deformation behaviors exist among the samples, namely, pore breakup, pore filling and pore coarsening.

II. Experimental Details

LPS of powder compacts were conducted aboard the Consort sounding rocket, three Space Shuttle missions and aboard Mir Station twice. The compositions were selected to yield different volume percent

of the liquid copper phase during sintering. The furnace module for these flights was configured to exceed the melting point of the additive materials (Cu in Fe-Cu and Co-Cu systems). The samples were processed for 2.5 minutes aboard the Consort 4 sounding rocket, 5 minutes aboard STS-57, 17 minutes aboard STS-60 and 66 minutes aboard STS-65, using the Equipment for Liquid Phase Sintering Experiments (ECLiPSE) flight furnace and quench system, described elsewhere [4]. The processing time for Mir station ranged from 10 minutes to 330 minutes.

The powders were used as received without further modification. They were weighed in air and blended in a rotary mixer. The mixed powders were transferred to a die lubricated with zinc stearate. A Carver hydraulic laboratory press was used to exert a compaction pressure. The pressed compacts were reduced in a tubular reactor under a flowing gas mixture of 5% H₂ with the balance He, following a time and temperature profile designed to remove contaminating oxides and lubricants. The samples were then separated by stainless steel or ceramic spacers and were put into ampoules that held the samples in the furnace [5]. The processed Co-Cu samples were analyzed using metallurgic microscope and Scanning Electron Microscope (SEM). The pore size was measured using IMAGEN Video Marking and Measurement System, SigmaScan Image Measurement System and Buehler's Omnimet Advantage Image Analysis System.

III. Pore Metamorphosis In Fe-Cu And Co-Cu Samples In Microgravity

1. Pore Breakup in Fe-Cu Samples

Examination of the samples taken from Fe-Cu system sintered aboard sounding rocket and Space Shuttle (STS-57, 60 and 63) showed that pores within the microstructure of the 30vol%Cu-Fe sample underwent metamorphosis, where larger pores broke up into strings of smaller spherical pores as the processing time increased [6]. Figure 1 shows that grains have coarsened considerably for the 30vol%Cu-Fe sample after 5 minutes processing; most networked pores had closed, and the pores were more spheroidized. More significantly, several of these individual spherical pores were linearly arranged. This suggests that they were originally part of ellipsoidal or cylindrical pores that were broken up by ovulation. Dumbbell shapes were also observed as a result of necking, suggesting that these pores were in the process of breaking up. Micrograph of the 30vol%Cu-Fe sample that was processed for 17 minutes showed additional pores arranged in linear strings, some of which were dumbbell shaped. The pore shapes were more spherical and much smaller in size. This strongly indicates that pores were breaking up and that the increased processing time resulted in pore of smaller sizes and regular shapes. Micrograph of sample processed for 66 minutes showed that the pore sizes and population did not change much as the

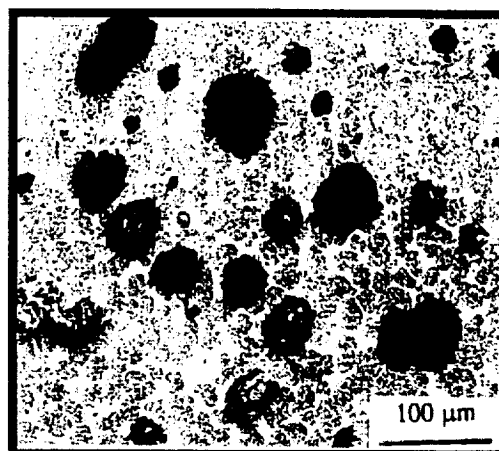


Figure 1. SEM-BEI Microphotograph of Fe-33Cu Sample Processed 5 minutes.

processing time was increasing from 17 minutes to 66 minutes. At the mean time, pore coarsening was also observed in samples with long sintering time. For high volume fraction samples, pore coarsening and pore filling was found instead of pore breakup [6].

2. Bifurcation in Pore Metamorphosis

To further study the pore metamorphosis with respect to sintering time and solid volume fraction, Fe-Cu and Co-Cu samples were processed aboard the Mir Station along with some Ag based compacts. Processing time up to 330 minutes with solid volume fraction ranges from 50% to 80%. Analysis of these samples showed that pores exist even when the samples are processed in vacuum [7].

The microstructures of Cu-Fe samples exhibited both pore breakup and coarsening during sintering process, based on liquid volume fraction. For low liquid volume-fraction samples, pore breakup dominants. Figure 2 shows a string of pores, which resulted from one pore, in 70vol%Cu-Fe sample. The center-to-center distance measured in this sample was about 2.5 times of the pore diameter. Figure 3 shows a pore undergoing breakup in 80vol%Cu-Fe sample. It can be seen that the condensed liquid copper is formed inside the pore to form bridges that broke the pore in several places. When this pore is fully isolated by the liquid copper, the pressure changes due to the surface tension will cause each small pore to shrink. As a result of pore breakup, the densification will be higher. As the liquid volume increase, the pore-size increases and the total number of pores decrease. For the 50vol%Cu-Fe sample, only a couple of pores left and one pore was larger than 2 mm in diameter. The densification data also showed that highest liquid volume fraction samples has lowest densification, whereas the 20vol% and 30vol%Cu samples showed the highest densification. This is the same as the densification changes in Fe-Cu samples processed in sounding rockets and Space Shuttle missions.

It is known that the Ostwald ripening influences pore size changes, where smaller pores will disappear and large pores grow even larger. However, from the densification point of view, the experimental results showed that pore breakup dominants in low liquid volume samples and pore coarsening dominants in high liquid volume fraction. For Fe-Cu system, the critical liquid volume fraction for pore behavior bifurcation is between 30% and 40%.

3. Solid Volume Fraction and Volume Diffusion:

Evidence of the pore metamorphosis from microgravity processed samples showed some snapshots of pore behaviors, which are otherwise obscured by gravity. In the last several decades, some

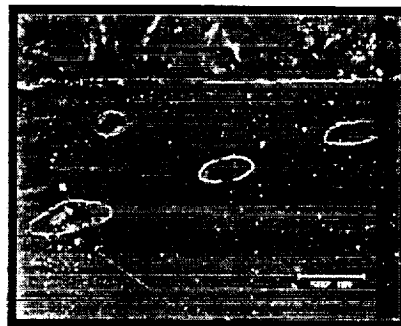


Figure 2 A String of Pores (30%Cu-Fe, Processing time 330 minutes).

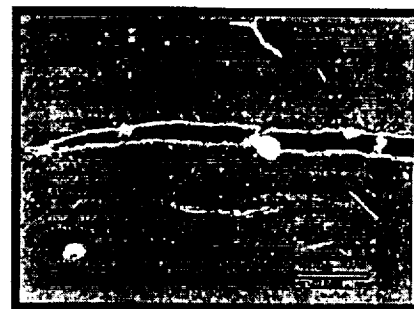


Figure 3 A Pore is Undergoing Breakup (20%Cu-Fe, Processing Time 330 minutes).

studies on morphological stability of pores have been published using Rayleigh's instability theory and bubble's fluid properties. Later in Moon and Koo's study [3] on bubble formations during solid phase sintering, mass transport during sintering was combined with instability theory. The microgravity processed samples more closely captured pore metamorphosis as evidenced by bifurcated behaviors based on the composites properties and surface free energy.

Moon and Koo studied bubble formation in solid phase sintering and showed that surface diffusion controlled bubble shape accommodation. They derived equations for the separation distance of pores in solid phase sintering based on Rayleigh's perturbation theory and determined that the equation for pore breakup by volume diffusion of vacancies resulted in $\lambda_m = 2.94d$, where d was the pore diameter following the breakup and λ_m is the center to center distance [3]. The surface diffusion and volume diffusion do exist in all LPS systems. It is obvious that the liquid bridges shown in Figure 3 couldn't be the result of liquid flow, but the result of volume diffusion. For this 20vol%Cu-Fe sample, because of the liquid wetting and dissolution on Fe particles (Cu has high solubility for Fe), and the strong capillary forces that prevents liquid Cu from flowing into the pore, no excess liquid can be further transferred into the pore. This results in a skeleton structure that prevents further breakup of the pores even after 330 minutes sintering. For 70vol%Fe-Cu sample, the excess of liquid makes it possible for pore to further breakup. However, because of the existence of particle agglomeration and relatively high solid volume fraction in this sample, solid diffusion does exist in 30vol%Fe-Cu samples. The governing equation for pore breakup due to the volume diffusion is described as [8]:

$$\frac{f_n}{f_t} = B \nabla_s^2 K \text{ with } B = \frac{D_s \gamma \Omega^2}{kT}$$

where D_s = volume diffusion coefficient (isotropic), γ = surface tension, v = number of diffusion atoms per unit surface area, Ω = Atomic volume, k = Boltzmann's constant, T = absolute temperature, $\nabla_s^2 K$ = surface Laplacian of K and K is the mean curvature of the surface.

The pore breakup due to the volume diffusion does not apply to the high liquid volume fraction samples. As the liquid volume fraction increases, the effects Ostwald ripening become dominant, which results in pore coarsening where small pores disappear and larger pores become larger.

The pore separation distances for various pore diameters were measured for Fe-Cu system and is shown in Figure 4. Following Gupta's treatment [9], only those spherical pores that appear to be regularly aligned after ovulation were considered.

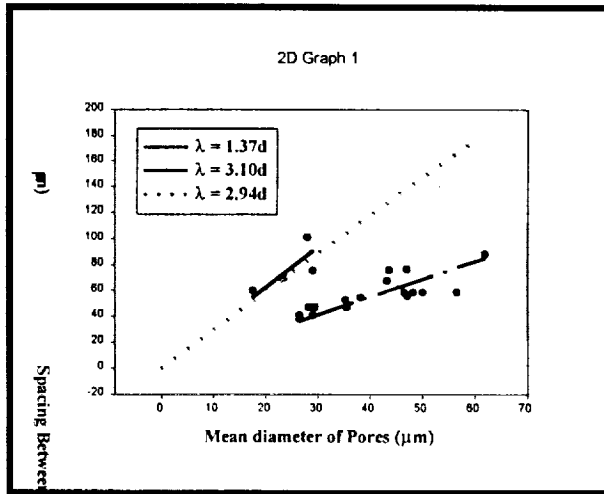


Figure 4. Center-to-Center Separation Distance between Spherical Pores vs. Diameter of Pores Following Breakup at Various Processing Times.

The data were taken from 30vol%Fe-Cu samples processed in Space Shuttle. The data can be interpreted as two parts. The dotted line shows the effects of volume diffusion because of particle agglomeration and the high local solid volume fraction in 30vol%Fe-Cu samples which provide a near-solid-phase-like sintering environment. The presence of solid particles within the liquid phase in contact with the pore interface also causes local solid phase sintering which enhances pore breakup by volume diffusion similar to what Moon and Koo has described. These particles significantly alter the capillary force action on the pore, and consequently the pressure distribution in the liquid surrounding the pore. For higher liquid volume fraction samples, solid sintering may also be enhanced by agglomeration of particles. The solid line in Figure 4 shows a bubble separation mainly caused by fluid properties inside the sample. A least square fit of the data gave a slope of 1.186d (Figure 4).

4. Grain Growth and Initiation Mechanism

Consider a pore that is surrounded by solid particles that bind together by capillary force driven agglomeration induced by the liquid phase. As the particles grow, the radii of the liquid meniscus between particles increase. As a result of this growth, a pressure difference draws liquid into the pore, thus reducing the pore radius and increasing densification [10]. It has been found that both Fe-Cu and Co-Cu showed pore filling in high liquid volume-fraction samples.

For the lower liquid volume-fraction samples, say 30%, non-uniform grain growth may lead to liquid flowing into the local meniscus and generate interparticle forces associated

with this flow. This will result in pore breakup. In this way some larger pores which cannot be filled due to the large pore radius can eventually undergo breakup at some point, depending on their initial size. To verify the liquid impact effect, a CFD code on bubble formation in a liquid

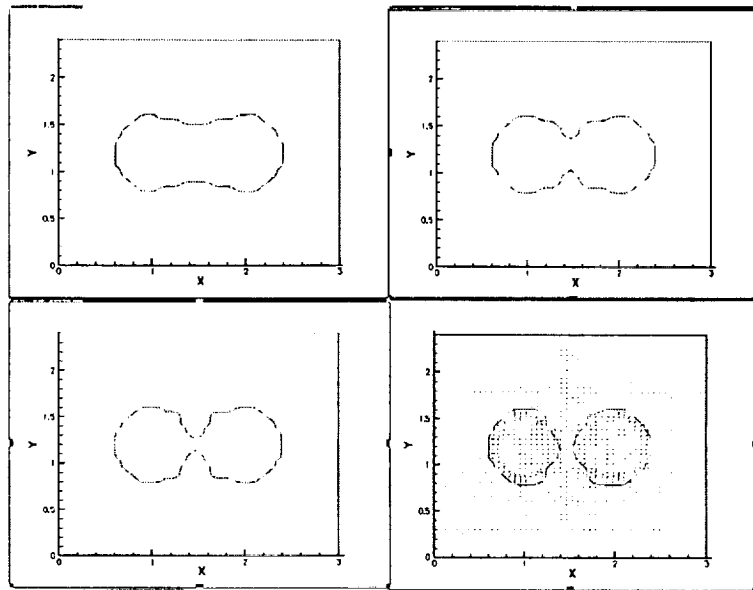


Figure 5 CFD Simulations on A Cylindrical Bubble Breaks up into Two Small Bubbles under a Initial Perturbation in longitude direction.

system was applied to the Fe-Cu system. The governing equation is described as:

$$\frac{f\bar{u}}{ft} + \bar{u} \left(\bar{u} = \frac{1}{\rho} \left(-P + \frac{\mu}{Re} \nabla^2 \bar{u} + \bar{F}_{st} \right) \right) \text{ with } \langle \bar{u} = 0$$

where F_{st} is the force associated with surface tension.

The results are shown in Figure 5, which shows a cylindrical bubble that breakups into two small bubbles under a vertical flow impact to the pore. The separation distance shows a nearly 1.2 times of the pore diameter. The solid line in Figure 4 shows a slope about 1.186. Given the influence of particle or the volume diffusion, it is reasonable to say that solid line is the result of the fluid mechanics that associated with grain growth.

V. Conclusion

Microstructure of Fe-Cu samples from microgravity processed samples showed that pore exhibited bifurcated behaviors based on their liquid volume fraction. At the beginning of liquid phase sintering, volume diffusion dominates in low liquid-volume fraction samples and broke the pore into pieces. The extreme case is the bubble formation in solid sintering. Liquid flow in higher liquid-volume fraction samples initiated by non-uniform particle growth also caused pore breakup, while otherwise lead to pore filling. Both pore breakup and pore filling in Co-Cu or Fe-Cu sample lead to higher densification.

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References

1. German, R. M., Liquid Phase Sintering (New York), Plenum Press, 1985.
2. D. R., Lide, Editor-in-Chief, CRC Handbook of Chemistry and Physics, 72nd Edition, CRC Press, Boca Raton, Ann Arbor, Boston, 1991-1992.
3. D. M. Moon and R. C. Koo, "*Mechanism and Kinetics of Bubble Formation in Doped Tungsten*", Metallurgical Transactions A, Vol.2, pp.2115-2122, 1971.
4. E. Atchley, T. Hamilton, A. Hedayat, J. G. Vandegrift, and J. E. Smith Jr., "*Overview and Preliminary Modeling and Ground-Based Results for the ECLiPSE*", 8th International Symposium on Experimental Methods for Microgravity Materials Science, TMS publication, pp. 87-94(Available in CD-ROM format only), edited by Dr. Robert A. Schiffman. 1996.
5. J. G. Vandegrift, Master thesis, University of Alabama in Huntsville 1996.
6. Z. Xue, J. G. Vandegrift, and A. K. Kuruvilla, "*Microgravity Liquid Phase Sintering and Pore Evolution*", Mater. Trans., JIM, 37, 1084-1090(1996).
7. S. Ye, A.K. Kuruvilla, Y. He and J. E. Smith, Jr., "*Optizone Liquid Phase Sintering Experiment (OLiPSE-01) (NASA 2 Final Research Report), Phase 1 Research Program Quarterly Research Report*", Sixth Quarterly Report, pp1-3 – 1-14, National Aeronautics and Space Administration, Lyndon B. Johnson Space Center, Houston, TX, August 1998.
8. F. A. Nicols and W. W. Mullins, "*Surface-(interface-) and Volume-Diffusion Contribution to Morphological Changes Driven By Capillary*", Trans. AIME, Vol. 233, pp.1840-1848, 1967.
9. T. K. Gupta, "*Instability of Cylindrical Voids in Alumina*", J. Am. Ceram. Soc., Vol. 61, pp. 191-195, 1978.
10. H. Park, S. Cho, and D. Yoon, "*Pore Filling Process in Liquid Phase Sintering*", Metallurgical Transactions A, Vol. 15A, 1984, pp1075-1080.

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